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Volume - 6

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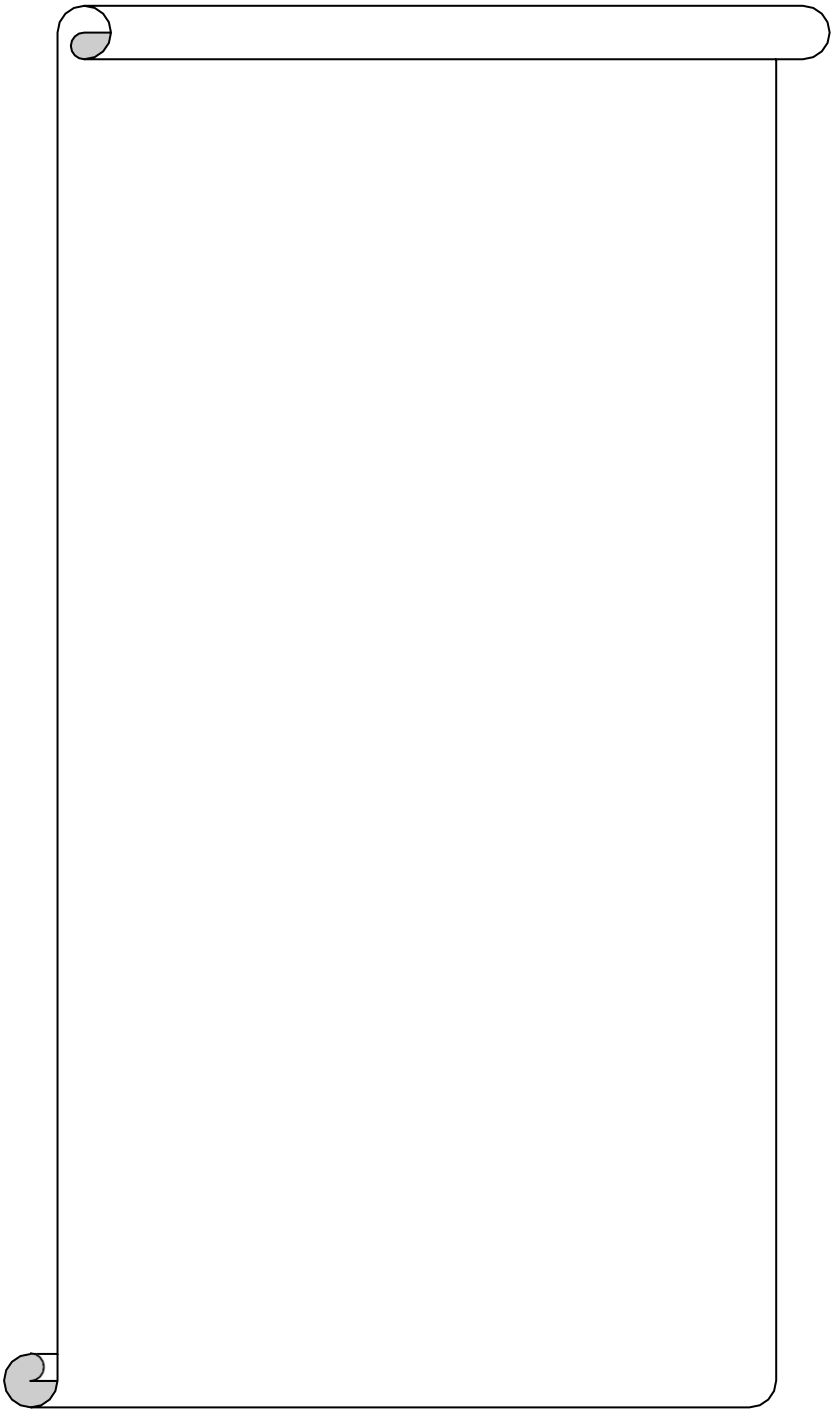

Chapter - 2
Impact of Whey Derived Bio-Active Components on Resolving Human Health Issues: As Nutraceuticals

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Chapter - 2

Impact of Whey Derived Bio-Active Components on Resolving Human Health Issues: As Nutraceuticals

Sonia Morya and Archibald Danquah-Amoah

Abstract

Milk is one of the nutritious source and extensively used for human consumption. India is biggest producer of milk and per day million of tonne of milk is produce and processed. Per day huge amount of whey generated from dairy industries. Whey is a nutritious byproduct that contains 45-55% of milk nutrients. In given chapter we are lighting up the impact of whey proteins in human health as whey proteins contains all essential as well as non-essential amino acids. Apart from nutrition, there is huge amount of data/information available which define the bioactive role of whey components in human health, including anti-cancer properties, helps in cardiovascular diseases, helps in weight reduction (obesity), helps in gastrointestinal health, hypertension (global public health issue). Research suggested that about 9 essential amino acids are found in whey protein, which are not synthesize by body and each amino acid has its own role in body metabolism. Therefore it's necessary to consume more essential amino acids to complete the requirement of body. Bearing in mind the nutraceutical significance of whey derived proteins, this chapter highlighted its recognized and emerging bioactive roles in human health issues.

Keywords: Whey proteins, nutraceutical, cardiovascular diseases, anti-cancer properties, health

Introduction

Milk is one of the nutritious source and extensively used for human consumption. It can easily get from number of domestic milking animals such as cow, buffalo, sheep, and goat. Fresh milk comprises approximately 80% casein and 20% whey protein, lipid, vitamins and necessary ingredients for growth (Foegeding *et al.*, 2002; Marshall, 2004). Whey is obtained during the process of preparation of cheese, paneer, channa and shrikhand where casein proteins coagulates due to the action of chymosin or organic

acid after the casein curd partitioned from the milk and watery thin liquid known as a whey (Sukumar, 2002) and whey known as a potent by-product of dairy industry. Whey is a nutritious byproduct that contains 45-55% of milk nutrients. It contains 20% of milk protein of which whey proteins are recognized as best quality protein with a protein efficiency ratio (PER) of 3.6 (Morya *et al*., 2017).

Whey has greenish or bluish color depends on the type or quality of milk used for whey manufacturing. It can be obtain from different types of milking animals like cow, buffalo, goat, sheep, and even from camels but most popular in western countries is of cow milk (Smithers, 2008). Whey is by-product of cheese, paneer and casein manufacture industry (Bulut and Akın, 2009). There is an increased awareness all over the world on the potential utilization of whey, primarily because of pollution, preventive regulation, and economic conditions. Whey and whey derived products besides being an excellent nutritional ingredient have a wide ranging and excellent functional characteristics supplying flavor, consistency, color and overall appearance in variety of foods (Morya *et al*., 2017).

During cheese processing there are two types of whey obtained sweet whey and acid whey. Sweet whey is resultant from the manufacture of rennet (enzyme) produced cheeses and acid whey is resultant from the manufacture of acid-produced cheeses. The composition of whey products varies according to the milk source, type of cheese, the methods of production, purification and concentration, and manufacturing process (Walzem *et al.*, 2002; Anonymous, 2003; Harper, 2004). Whey proteins accounts 20% of total milk protein are also a heterogeneous, polymorphic group of proteins composed of lactalbumin (LA, 20%), lactoglobulin (lg, 50%), bovine serum albumin (BSA, 10%), immunoglobulin (10%), and proteose & peptones (10%) (William, 2004).

Khamrui and Rajorhia (1998) suggested that around 2 million tonnes of whey generates annually with 130,000 tones of valuable milk nutrients. Nowadays, whey protein is developing into a single-out after product and it gives functional properties to food. Whey is not only the source of protein but it contains other valuable dairy constituents as well like lipid e.g. conjugated linoleic acid [CLA], minerals, and lactose (milk sugar) which provides energy as it a form of carbohydrate along with this it also act as a probiotic which promote the growth of beneficial bacteria.

Whey is a precursor for some bioactives such as lactulose and lactobionic acid. It has a relatively low glycemic index and low

cariogenicity. Even though in whey lipid concentration is low, the bioactivities of sphingomyelin (a phospholipid) and conjugated linoleic acid are impending health improving ingredients (Vesper *et al.*, 1999; Belury, 2002; Walzem *et al.*, 2002; Anonymous, 2003; Harper, 2004).

Profile of Essential and Non-Essential Amino Acid Content of Whey Proteins

Bovine milk proteins (casein and whey) are good source of essential as well as non-essential amino acids, that's why considered as complete source of amino acids. Research suggested that about 9 essential amino acids are found in whey protein, which are not synthesize by body and each amino acid has its own role in body metabolism. Therefore it's necessary to consume more essential amino acids to complete the requirement of body.

Proteins of milk are the major source of immunological bio active peptides (Coker *et al.*, 2012; Burd *et al.*, 2011). Leucine, isoleucine and valine etc. are the example of branched chain amino acids which are abundant in whey proteins, and branched chain amino acids (BCAA) are takes part in various metabolic reactions and accounts one-third part of muscle protein therefore involves in protein synthesis. Consumption of branched chain amino acids (BAAs) before the exercise results in high uptake in muscle tissues and brings many advantages like lower the levels of lactate with improvement in muscular oxidation; boost up the circulation of growth hormone; lower the concentrations of intramuscular enzymes.

Branched chain amino acids are accountable for these factors and results in muscle recovery and less damage (Luigi *et al*., 2016; De Bandt and Cynober 2006). Gut and liver degrades these amino acids as well as other amino acids, and we can say that, branched chain amino acids (BCAA) are constantly released into skeletal muscle from the liver and other internal organs and helps in controlling blood sugar levels and showed 40% blood sugar production indeed, branched amino acids may be responsible, and showed up to 40% (approximately) of blood sugar production for the duration of exercise (Luigi *et al*., 2016; De Bandt and Cynober, 2006). Studies showed that, whey protein helps in boosting the immunity by intracellular transfer to glutathione, as they contain sulphur rich amino acids like cysteine and methionine.

Whey Protein Components and Their Functionality

Whey is rich source of nutrients in which whey proteins consist of several different proteins including alfa-Lactalbumin, beta-Lactoglobulin, bovine serum albumin, heavy and light chain Immunoglobulins (Igs),

lactoferrin (LF), lactoperoxidase, and glycomacropeptide (GMP) (De Wit, 1998). Whey proteins are rich in proteose and peptone with low molecular weight products which are formed by the process of enzymatic degradation of the caseins (milk protein) during the cheese making process (De Wit, 1989). Whey contains 20 amino acids, in which nine are essential amino acids due to this reason biological value of whey protein stands higher in compared to other sources of protein (Shah, 2000). In comparison to vegetable protein sources whey proteins has higher value of all essential amino acids (Walzem *et al.*, 2002).

Proteins of whey dissimilar of casein protein and thus have high levels of secondary, tertiary, and quaternary structures. Whey protein structures are stabilizes by intermolecular disulfide bonds. The leading proteins of whey are alpha- lactalbumin, beta-lactoglobulin, which are responsible for functional properties of whey (William, 2004). Whey proteins also hold bioactive substances such as growth factors, cytokines, and hormones, which have physiological role to regulate cell growth in both normal cells and tumor cells by suppressing proliferation (Morr, 1989; Sukkar and Bounous, 2004).

Many biological activities of whey proteins are acknowledged including digestive functions, gastrointestinal functions, hypertension and gastric blood flow, anti-carcinogenic properties, analgesic properties, growth factors, immune-regulatory, and non-immune disease resistance (William, 2004). Table 1 shows the different characteristics of sweet whey and whey permeate in terms of specific gravity, pH, titrable acidity, water etc.

Table 1: Characteristics of whey (Gupta and Dhan, 2017)

Characteristics Chemical Composition	Sweet Whey	Whey Permeate
Specific gravity (kg/L)	1.025	1.030
pH	6.40	6.55
Titrable acidity (%)	0.05	0.089
Water (%)	91.95	94.45
Dry matter (DM %)	8.05	5.55
Solid not fat (SNF %)	7.55	5.55
Fat (%)	0.50	0.00
Crude protein (CP %)	1.10	0.25
Soluble carbohydrates (%)	5.20	4.90
Total ash (%)	0.52	0.50

Table 2: Amino acid content per 100 gm (McDonough *et al.,* 1974)

Essential Amino Acid	Whey	Casein	Breast Milk
Isoleucine	5.75	4.7	0.056
Leucine	12.32	9.0	0.095
Lysine	10.32	7.4	0.068
Methionine	2.11	2.6	0.021
Phenylalanine	3.85	4.9	0.046
Threonine	5.83	4.1	0.046
Tryptophan	2.58	2.1	0.017
Valine	6.13	6.4	0.063
Non-Essential Amino Acids			
Histidine	2.15	2.7	0.023
Alanine	5.15	2.9	0.036
Arginine	3.25	3.4	0.043
Aspartic acid	11.68	6.6	0.082
Cysteine	2.36	0.4	0.019
Glutamic acid	17.28	21.2	0.168
Glycine	1.8	1.7	0.026
Proline	4.79	10.1	0.082
Serine	5.15	5.5	0.043
Tyrosine	3.23	5.3	0.053

A) α-Lactalbumin

One of the chief whey protein found in human and bovine milk, i.e. alpha-lactalbumin which accounts ant proliferative effects in human cell lines especially in case of adenocarcinoma. It has antimicrobial activity against *E. clostridium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Staphylococcus epidermis*, *Streptococci*, and *C. albicans.* Allergy is a serious problem for young children who are regularly able to use or consumed goat milk without suffering that reaction. Different percentage of alpha lactalbumin is present in animal to animal e.g. cow (52.9-53.6 %); goat (13.31-34.7%), sheep (8.97-17%), and human (30.3-45.4%) (Ren, 1993; Kelleher, 2003; Potoctnik, 2011). According to reliable sources, alpha-lactalbumin generally found much higher in cow's milk in compare to other milk animals and studied many cases of allergic response in many human beings (Ren, 1993; Kelleher, 2003).

α-Lactalbumin is a whey protein which is rich in cysteine, the essential amino acid (EAA), which has a key role in the biosynthesis of glutathione, having properties of antioxidant, anti-carcinogenic, and immune stimulatory effect and plays an important role in the regulation of whole body protein metabolism, which results in changes in body composition (Bounous *et al.,* 1989; Walzem *et al.,* 2002). It creates about 25% of total whey protein part and includes an ample range of amino acids, together with a readily available supply of essential amino acids and branched chain amino acids.

Nowadays purified α-lactalbumin is widely used in food industries to prepare infant formulas to make them more alike to human milk (Walzem *et al.*, 2002; Heine *et al.*, 1996), suggested to addition of extra alpha-lactalbumin in infant food in cow milk based formula so good balance of amino acids can be achieve by the producers, because in average infant formula there is excess of lysine and methionine and insufficiency of tryptophan and cysteine. The uses of other components of whey and milk proteins (LF, lactoperoxidase, β-casein, and GMP) have also been designed for infant foods (Jost *et al.*, 1999).

However, due to high cost processing reason, the majority dairy based infant formulas contain constituents such as demineralized whey with higher levels of β-lactoglobulin, cause them less alike to human breast milk (Marshall, 2004). Alpha-lactalbumin also binds calcium, zinc and other minerals with stress reduction, anticancer, antimicrobial, and antiviral activities, and immunomodulation (Walzem *et al.*, 2002). Alpha-lactalbumin enriched whey protein meal preserves lipid oxidation and decreases adiposity in rats (Bouthegourd *et al.*, 2002).

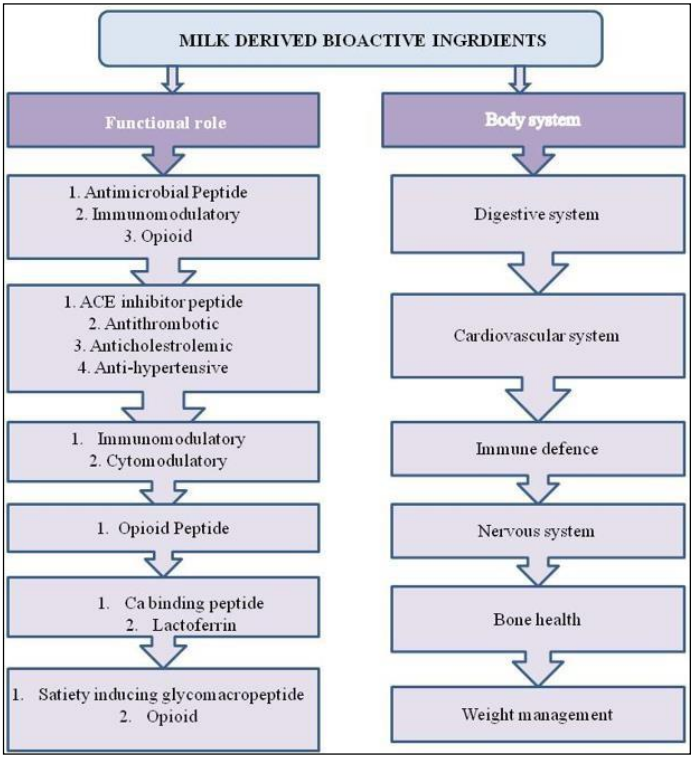

Fig 1: Milk-derived bioactive peptides and their physiological functionalities

B) β-Lactoglobulin

Milk is rich source of proteins and whey protein is one of the major protein out of two found in the milk, and we all knows that beta-lactoglobulin is a major part of whey protein and accounts about half of total whey protein. Study says that beta-lactoglobulin didn't found in human breast milk but easily recognize in whey proteins of mare, goat, and sheep milk (Le Maux, 2012). It plays an important role in availability and absorption of vitamin A as it can bind retinol. Beta-lactoglobulin is a good natural source of essential amino acids (EAA) and branched chain amino acids (BCAA) (Guimont *et al.,* 1997; Walzem *et al.,* 2002; Harper, 2004).

Le Maux *et al.,* delineated that the bio-accessibility of linoleate and linoleic acid is alters by the beta-lactoglobulin as it acts as a carrier molecule in the process (Le Maux *et al.,* 2012). It also supplies confrontation against gastric and simulated duodenal digestions. It also provides a possible carrier for transporting gastric labile hydrophobic drugs. Thus it has a vast potential to give out a realistic protein aspirant for safe delivery and safety of pH-sensitive drugs in the stomach (Mehraban *et al.,* 2013).

The available percentage of beta-lactoglobulin is accounted in sheep 59.24 -77.7%, in goat 43.54-63.8% and in cow (18.4-20.1%). This protein contains anti-hypertensive peptides which are answerable for decline in blood pressure and also prove considerable effect on angiotensin converting enzyme inhibitors. Nearly all of the valuable effect related to peptides formation during the hydrolysis of whey proteins. These whey protein peptides is one of the major peptides that are answerable for hindering angiotensin converting enzyme, which stimulates blood-pressure regulating effects (Le Maux *et al*., 2012).

C) Lactoferrin

Lactoferrin is a protein which naturally found in human breast milk, tears of eyes, bile juice, blood, saliva, and mucus. It is a iron binding glycoprotein which consists of about 689 amino acid residues and concentration of it in human milk is 2mg per ml, and in colostrums 7mg per ml respectively; although in bovine milk 0.2mg per ml, and in colostrums 1.5mg per ml respectively (Gupta and Chaphalkar, 2016).

Lactoferrin, mechanisms of anti-microbial effects have been established (Farnaud & Evans, 2003), and presently figure a sound foundation for the application of this protein in improving the safety measures of meat (Naidu *et al.,* 2003). It has been proved experimentally that lactoferrin possess numerous bioactive properties which helps in reducing certain health

problems. The bioactive role of lactoferrin appears to be dependent on exceptional iron-binding activity by the molecule. Iron balance studies conducted to evaluate iron availability in infant formula containing bovine milk lactoferrin (Schulz-Lell *et.al.,* 1991). Research in uses of lactoferrin regularly going on, and in market many food products are available incorporating with recombinant human lactoferrin and bovine lactoferrin which enhance our immune system with antiviral and antibacterial activities against pathogenic microbes in our intestine (Gupta, 2016).

Study says that, lactoferrin arrives in the lower bowel after surviving in stomach and small intestine and sequester iron from bacteria in lower bowel, in view of the fact that pathogens need high amount of iron for their metabolism of growth, and property of sequestering of iron from pathogens makes lactoferrin antimicrobial. Lactoferrin exhibit both characteristics inhibition of pathogens as well as growth of lactobacilli.

D) Glycomacropeptide

Glycomacropeptide now a day used in functional foods and pharmaceuticals as a potential ingredient (Martin-Diana *et al.,* 2006; Nakano *et al.,* 2006; Thoma-Worringer *et al.,* 2006). GMP is a casein-derived during cheese-making and free into whey due to the act of the enzyme (chymosin), on κappa-casein. GMP is also called caseinomacropeptide. This protein accounts 10-15% of whey. This protein has antibacterial, antiviral, and immunomodulatory activities, as well as prebiotic effect to promote the growth of bifidobacterium. Due to the absence of aromatic amino acids, phenylalanine, tryptophan, and tyrosine GMP is used to formulate foods for patients with the disease phenylketonuria (Brody, 2000; Shah, 2000; Walzem *et al.,* 2002; Anonymous, 2003a; Harper, 2004). GMP addition has also been proposed for use in newborn baby formula (Jost *et al.,* 1999).

E) Lactoperoxidase

Milk whey contains various types of enzymes like hydrolases, transferases, lyases, proteases and lipases, and one of the another bioactive enzyme name lactoperoxidase has bactericidal effects against bacteria (De Wit, 1998). It is the most profuse bioactive enzyme found in whey. Lactoperoxidase, bioactive whey protein also used in infant formula (Jost *et al.,* 1999). It acquires about 0.25-0.50% of total whey protein, and it helps in many reactions like, regulating the level of hydrogen peroxide, catalyzes some molecules, and catalyzes peroxidation of thiocyanate, and some halides like iodine and bromium, which are responsible for inhibitory effects against bacteria. Due to the bactericidal efficacy it act as antimicrobial agent and

used in dental products as a cavity inhibitor and suppress the growth of microbes (Bjorck, 1978; Kussendrager *et al.*, 2000; Anonymous, 2003a; Harper, 2004). During the heat pasteurization process, lactoperoxidase not get deactivated hence suggesting its stability as a preservative.

Lactoperoxidase makes strong digestive system of neonatal babies by killing pathogenic microbes present in their digestive system. This enzyme plays an important role as innate-immune system in mammals and catalyzes the oxidation of the thiocyanate ion into the antibacterial hypothiocyanite (Reiter and Perraudin, 1991). The biological consequence of LPO enzyme is that it has a natural protection system against the attack of microorganisms. In addition to its antiviral effect, it cares for animal cells against different damages and peroxidative effects (De Wit and Van Hooydonk, 1996). Lactoperoxidase action of natural antimicrobial is being exploited in oral healthcare products (Boots and Floris, 2006), and getting application in the prevention and treatment of xerostomia (dry mouth) (Tenovuo, 2002; van Steenberghe, Van den Eynde, Jacobs, and Quirynen, 1994).

Studies showed that, the oral intake of lactoperoxidase (LPO) attenuated pneumonia in influenza virus-infected mice concealed the penetration of inflammatory cells in the lungs (Shin *et al.*, 2005). Therefore, the major function of lactoperoxidase is a defending factor against infectious microorganisms. The lactoperoxidase holding products have been clinically confirmed to hinder harmful microorganisms linked with gingivitis and oral irritation, to support the healing of bleeding gums and reduce inflammation, and to fight both the causes and effects of halitosis (bad breath) (Tenovuo, 2002).

F) Bovine Serum Albumin

Bovine serum albumin is a large bioactive protein of whey that makes up around 10-15% of total whey protein. Bovine serum albumin is a source of essential amino acids (EAA) and carrying insoluble free fatty acids (De Wit, 1998). There is a very less literature available regarding its possible therapeutic activity. It is indistinguishable to blood serum albumin (De Wit, 1998). Bovine serum albumin has also been used as natural matrix materials for delivery devices (Brannon-Peppas and Peppas, 1991). Bovine serum albumin (BSA) may exhibit anti-carcinogenic activity (Laursen *et al*., 1990). It has also been projected for use in newborn formula (Jost *et al.*, 1999). Bovine serum albumin (BSA) is a large bioactive protein found in milk. It consists of about 2-5% of whey protein. Bovine serum albumin protein has a high concentration level of sulphur amino acids and glutamylcysteine, both of which are precursors for glutathione (Bounous, 2000).

Glutathione is an enormous antioxidant made by the body and has ability to reprocess other antioxidants for reused by the body. Glutathione is very important antioxidant, if concentration of it low in body that indicates poor health (Kharb *et al*., 2000). Bovine serum albumin may well protect mammalian cells against certain genotoxic agents (Bosselaers *et al*., 1994). Bovine serum albumin has important role to inhibit tumor growth. *In vitro* cell culture, Bovine serum albumin (BSA) suppresses an estrogen responsive breast cancer cell line, MCF-7, (Laursen *et al*., 1990). The cancer growth was inversely proportional to concentration of bovine serum antioxidant. A recent research concluded that ribosylation of BSA outcome in reactive oxygen species (ROS) accumulation which destroyed breast cancer cells (Khan *et al.,* 2013).

G) Immunoglobulins

Immunoglobulins characterize the most plenteous of the conventional bioactive proteins found in whey, while colostrum characterizes the favorite choice for the manufacture of immunoglobulin enriched milk products (Huffman and Harper, 1999), cheese processed whey has been used for the manufacture of alike ingredients (Ayers, Elgar, and Pritchard, 2003). These immunoglobulin loaded isolates all convey passive immunity to the end user, and proof is construction that they combat infections, improve athletic performance and healing times, support those who may be immune compromised, and increase gut health (Buckley *et al.,* 1998; Coombes *et al.,* 2000; Mehra, Marnila, and Korhonen, 2006; Mero *et al.,* 1997; Playford *et al.,* 1999).

Many studies has claimed that several components especially immunoglobulins be present in whey protein that are accountable for improving its immunity. The maximum concentration of these immunoglobulins is still found in colostrum (immune rich). As per the literature, Immunoglobulins exists in the form of antibodies i.e. IgG, IgM, IgA, and Secretory IgA; Ig stands for Immunoglobulin, in whey proteins that are advantageous for the dealing of various bacterial infections (Bell, 2000).

In other words, these immunoglobulins provide passive maternal immunity to newborn babies through breast milk and facilitate to uphold our immune system. Overall, immunoglobulins confirmed significant 10-15% of total whey proteins derived from bovine milk. Out of these immunoglobulins, IgG has been found at concentrations of 0.6-0.9 mg/ml in bovine milk. Other studies also says that raw milk from non-immunized cows include specific antibodies against *E. coli*, *Salmonella enteritidis*, *S. typhimurium*, *Shigella flexerni* and human rotavirus (Bell, 2000). In one of

the studies related to lactoferrin content in milk samples of different animal species i.e. cow, sheep and bovine. The research results showed that colostrums (milk after calving) produced much higher lactoferrin content followed by goat, sheep and bovine (Gupta and Chaphalkar, 2016[a]; Gupta and Chaphalkar, 2016[b]).

Therapeutic Indications

Effect against Carcinogenesis

So many studies in the area of anti-cancer properties of whey have already done as well as running, and results that lactoferrin and glutathione (GSH) are primarily allied with the immune modification, antioxidant properties, detoxifying properties (Marshall, 2004).In the existence of lactoferrin, the metastasis of primary tumors in mice was inhibited while colon cancer in rats demonstrated reduced tumor expression (Sekine, 1997; Yoo, 1998). In some *in vitro* researches results showed that in breast cancer case inhibition of few significant steps recognized when treated with bovine serum albumin (BSA) protein, even though the mechanisms were not fully implicit (Yoo, 1998). In few clinical study trials proposing high level of glutathione in tumor cells confer confrontation to chemotherapeutic agents.

In one of these studies few patients with stage IV malignancies were prescribed with 40 g whey in combination with supplements such as ascorbic acid and a multi-vitamin/mineral formulation for 6 months and maximum were demonstrated with increased levels of natural killer cell function, GSH (glutathione), hemoglobin, and hematocrit (Yoo, 1998). An insistent combination of immune dynamic nutraceuticals was effective in extensively increasing natural killer function, other immune factors, and plasma hemoglobin in patients with last stage cancers. Data is growing that particular whey derived proteins and peptides & proteases have potential anti-cancer effects against certain tumors (Bounous *et al*., 1991; Gill and Cross, 2000).

The majority proof to date has been based on *in vitro* cell culture, *in vivo* animal studies, and some epidemiological researches. For example, in work reported by Mcintosh *et al.*, (1995) and Hakkak *et al.*, (2001) whey protein diets were shown to be more effective than other dietary proteins (casein, meat, and soy) in reducing the frequency and burden of colon tumors in a rat model of the disease.

Effect against Cardiovascular Disease

A number of studies say that ingestion of milk and milk products can lower the blood pressure level and minimize the threat of hypertension

(Marshall, 2004). Kawase *et al.*, carried out 8 weeks research trial in which 20 fit men were given a combination of fermented milk and whey protein concentrate and then study the effect on serum lipids and blood pressure (Kawase *et al.*, 2000). After the completion of 8 weeks, the fermented milk group verified relatively higher HDL (high-density lipoproteins), lower systolic blood pressure, and lesser triglycerides. In obese young men cardiovascular risk factors were examined and effects of whey protein supplement and resistance training on antioxidant status tested (Sheikholeslami and Ahmadi, 2012). Conclusions recommended the synergistic effect of resistance training and whey consumption as manifested in higher total antioxidant capacity, glutathione and HDL levels.

Effect against Gastrointestinal Disease

Rosaneli *et al.,* delineated whey derived proteins exercise a beneficial effect on the gastric mucosa due to the presence of sulfhydryl group in amino acid cysteine and its linkage with glutamic acid in the production of glutathione (Rosaneli *et al.,* 2002), it was experimental that when rats showed a 41% decrease in ulcerative lesions caused by ethanol intake when they were fed a whey protein concentrate, while a 73% reduction rate was observed following repeat doses of whey (McGregor and Poppitt, 2013).

Whey derived proteins are absorbed faster than casein in body. Due to the low pH conditions in the stomach the absorption rate of casein is lesser in its native micellar form that causes casein clotting and postponement of gastric emptying (Dangin *et al.,* 2001). Hence, plasma amino acids are more swiftly elevated following whey proteins consumption; whereas changes in plasma amino acids are lower and more constant following micellar casein consumption. Thus, processing of whey proteins or casein fractions through hydrolysis can noticeably control absorption and following plasma amino acid profiles.

Whey mucosa-protective properties have been confirmed in numerous animal research studies and are possible to be related with its GSH stimulating properties (Marshall, 2004). It play an important role in synthesis of glutathione (GSH), the amino acid glutamate may play an additional role when it is changed to glutamine, an amino acid utilized as a energy by intestinal mucosa (O'Dwyer, 1989).

Effect against Hypertension

Hypertension is a most important global public health issue, and its definite treatment will possible to decrease the risk of cardiovascular diseases. A number of investigators have believe that certain bioactive

peptides formed through the hydrolysis of food proteins have the ability to inhibit ACE, and this subject has been broadly reviewed in a number of studies (FitzGerald, 2004; Pal, 2010; Kawase *et al.*, 2000; Sharpe *et al.*, 1994; Meisel, 2005; Korhonen, 2007; Silva and Malcata, 2005; Vermeirssen *et al.*, 2004; Xu *et al.*, 2008).

Generally, it has been proposed that a diet loaded with foods containing antihypertensive peptides is helpful for the prevention and treatment of hypertension. Angiotensin converting enzyme (ACE) inhibitor bioactive peptides may be obtained from precursor food proteins through enzymatic hydrolysis, the use of viable or lysed microorganisms, or specific proteases (Korhonen, 2003; Hartmann, 2007; FitzGerald, 2004). Nevertheless, studies involving to whey peptides with angiotensin converting enzyme (ACE) inhibitor activities are more limited; this may perhaps be due to the rigid structure of beta-lactoglobulin, which makes it principally resistant to digestive enzymes.

Angiotensin converting enzyme (ACE) inhibitor peptides can decrease blood pressure in a process regulated, in part, by the renin-angiotensin system; renin is a protease, which is secreted in response to various physiological stimuli that cleave the protein angiotensinogen to produce the inactive decapeptide angiotensin I. In addition, ACE acts on the kallikrein-kinin system, catalyzing the degradation of the nonapeptide bradykinin, which is a vasodilator (Kang, 2003), and angiotensin converting enzyme (ACE) inhibitor peptides exert a hypotensive effect by preventing angiotensin II formation and the degradation of bradykinin.

Effect against Osteoporosis

As Caroli *et al*., reported in a recent review on dairy intake and bone health, there are complex relationships between milk and dairy foods and osteoporosis (Caroli *et al.*, 2011). Milk basic protein (MBP) is a constituent of whey that reveals the capability to not only hold back bone resorption but also stimulate proliferation and differentiation of osteoblastic cells (Marshall, 2004). Milk protein primarily contains lactoferrin and lactoperoxidase. Animal studies recommend that lactoferrin may be the key active element, mediating its special effects through two main pathways: LRP1, a low-density lipoprotein (LDL) receptor–related protein that transfers lactoferrin into the cytoplasm of primary osteoblasts via endocytosis, and p42/44 MAPK, which stimulates osteoblast activity (Naot *et al.*, 2005).

The role of calcium intake in determining bone mineral mass is well

recognized to be the most critical nutritional factor to achieve optimal peak bone mass; milk protein is also important for preventing osteoporosis. A number of clinical trials support milk protein's positive effects in both men and women, the latter ranging in age from young to postmenopausal. Daily doses of 40 mg Milk basic protein (MBP) (equivalent to 400–800 ml milk) appear to be sufficient to significantly increase bone mineral density and reduce bone resorption (Toba *et al*., 2001; Seto *et al.,* 2007; Uenishi *et al.,* 2007).

Prebiotic Properties and Gut Functionality

Whey is a good source of prebiotic. In whey lactose (Carbohydrate) supports the growth of lactic acid bacteria like lactobacillus and bifidobacteria. Oligosaccharides such as stallic acid found in whey are usually attached to protein and exhibit prebiotic activity. In addition, there are three non-carbohydrate found in whey act as prebiotic. 1) Glycomacropeptide (GMP) helps in growth of bifidobacteria; 2) Calcium in form of calcium phosphate stimulate the growth of lactobacilli and helps to reduce the harshness of Salmonella infectivity in rats; 3) Lactoferrin (Lf) is third one whey component which act as prebiotic and it stimulate the growth of bifidobacteria and lactobacilli (Kassem *et al.,* 2015).

Impairment of gut function generally define as deferred gastric emptying, irregular motility patterns, and fragile intestinal barrier and results in a severe issue in seriously ill patients. Recommendation of whey protein fortification may impart inflammation and get better tolerance towards enteral nutrition (Abrahao, 2012).

Conclusion

From the above discussion, it is concluded that whey possess bioactive components which has remarkable therapeutic as well as nutraceutical properties, such as anti-cancer, immune-enhancer, prebiotic property, antimicrobial activity, cardiovascular, gastro-intestinal activity, physical, obesity control and weight-management, osteoporosis, hypertension. There are several whey-based probiotic products available in the market today that can dish up as attractive health-promoting food supplements. Whey based beverages, whey based probiotic beverages, yakult, kefir, yogurts, frozen yogurts, and desserts are best examples of whey rich food products. We should incorporate these probiotic rich products in our diet to accelerate our immune power.

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