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Review Article

Whey protein and its application to human

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Abstract

Proteins are complex macromolecules made up of amino acid which is essential for the biological activities. The coagulation of milk creates whey protein having the high nutritional value. This article discusses and summarizes important work in literature in response to the composition and production of whey protein. In this communication we reviewed the medicinal value of whey in various diseases like cancer, hepatitis, HIV and cardiovascular diseases. The role of whey protein in blood pressure and inflammatory response were also discussed. Its significance in human health particularly in sport performance was highlighted. Much stress was given to explain its role on satiety, adiposity and general health. Morever biotechnological prospective of whey protein was also explained. This article will be helpful for the biotechnologist working in the field of dairy which finally affects the human health.

Keywords: Protein, Whey, Disease, Human health

Introduction

Around 5000 BC, animal milk is first known to have been used as human food during the secondary products revolution. Whey is a protein, left over part when milk coagulates. It contains the soluble portion of milk and is 5% solution of lactose in water. Liquid whey has long been known to contain proteins of high nutritional value (Ling et al, 1961). In other words whey proteins are collection of globular proteins (McKenzie, 1971). Whey and whey-derived bioactive compounds have been studied for their ability to enhance general health and well being (Shah, 2000). Curd and whey are separated during the process of cheese making. The left over liquid after the milk is been curdled is whey (Krissansen, 2007). The amino acid composition of proteins present in whey posses high biological value. Besides, this protein show fundamental functional properties, which enable a varied application in foods, dietetics and beverages in form of different whey products like powder, protein concentrates and isolates (Barth and Behnke, 1997). Whey proteins are well known for their high nutritional value and versatile functional properties in food products. Estimates of the worldwide production of whey indicate that about 700,000 tones of true whey proteins are available as valuable food ingredients. Nutritional and functional characteristics of whey proteins are related to the structure and biological functions of these proteins. During recent decades, interest has grown in the nutritional efficacy of whey proteins (de Wit, 1998).

This article is based on literature survey. The authors explained the composition and specific advantages of the component of whey protein. The roles of the various proteins and peptides found in whey are highlighted. The production of whey protein from milk was also described in detail. As the whey protein has medicinal value so its role in different diseases was also discussed. Moreover the role of this protein on human health was also surveyed. Biotechnological prospect were also reviewed.

This article will be beneficial for those readers working with milk and milk products. It will provide significant knowledge for those who have adopted milk in their regular diet. Moreover the readers will know the significance of those milk products which are often discarded. This will help them for proper utilization of milk and its product. This article will help them to explore the significance of milk products in their daily life.

Composition of whey

Milk is a translucent white liquid produced by the mammary glands of mammals. The exact components of raw milk vary by species, but it contains significant amounts of saturated fat, protein and calcium as well as vitamin C. Earlier studies has described the day-to-day variations in milk components from cow (Forsbäck et al., 2010). As whey is the left over part of milk when it coagulates, it indicates to be composed of a number of proteins, peptides and other compounds. The important components of whey are listed in Table 1. Moreover the advantages of the components are listed in Table 2.

S. No.	Components
1	Beta- lacto globulin
2	Alpha-lacto albumin
3	Serum albumin
4	Immunoglobulins
5	Lactoferrin
6	Glycomacropeptide
7	Several amino acids importantly cyestine and leucine

Table 1: Components of whey protein

Table 2: Specific advantages of whey component

S. No	Component`s name	Specific advantage	References
1	Cysteine	Cysteine possesses a thiol group that acts as potent reducing agent and checks tissue damage and oxidation.	(Marshall, 2004)
2	Beta-lacto globulin	Contains large percentage of branched chain amino acids which act as fuel for the working of muscles and brain and also inhibits allergy.	(Krissansen, 2007)
3	Alpha-lacto albumin	Lactoalbumin is an immunostimulator. It reduces oxidative stress by chelating heavy metals. Moreover, administration of whey orally protects rats against ethanol and stress induced mucosal injury indicating its ulcer preventing activity.	(Wong et al. 1997) (Matsumoto et al., 2001)
4	Leucine	Leucine plays an important role in initiating the transcription pathway leading to protein synthesis. It is an important factor in tissue growth and repair.	(Marshall., 2004)
5	Glycomacropeptide	Glycomacropeptide stimulates the synthesis and release of hormone cholecystokinine in duodenum which helps in the digestion process.	(Beucher et al., 1994)
6	Immunoglobulins	Provides prophylactic protection against rotavirus and Helicobacter pyroli.	(Korhonen et al., 2000)
7	Bovine serum albumin	Close to about 9 essential amino acids are present in bovine serum albumin which helps in the normal functioning of the body.	(Krissansen, 2007)
8	Lactoferrin	It works by inducing programmed cell death, suppressing angiogenesis and by modulating carcinogen metabolizing enzymes. It also works as a iron scavenger.	(Parodi, 2007) (Krissansen, 2007)

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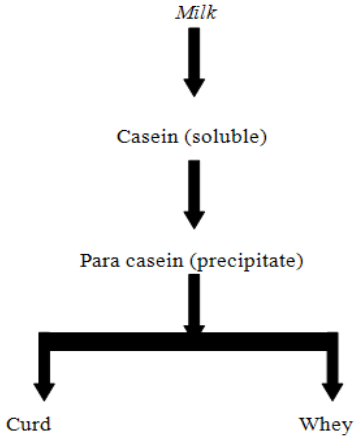
Production of whey

The milk we obtain from cow has several chemical compounds natively, that can be processed into several novel milk products. The most ancient approaches involve the formation of cheese from milk. The component of milk, casein is responsible for the formation of cheese. Casein is a soluble protein. Here by the enzymatic action of rennet the "glycopeptides" from casein structure is removed making it insoluble or in other words clotting it; forming paracasein. This paracasein along with calcium ions further transform into curd, leaving behind the supernatant which is called as whey (Fig 1). The precipitate obtained above is further used for the production of cheese. Milk whey is an abundant by-product in cheese manufacturing process. About 9 liters of whey can be produced from 10 liters of milk (Manso et al. 2004). Industrially starter culture of Streptococci or Lactobacilli is used at about 32^0 C for 10-75 minutes. Further processing gives a fine yield of cheese.

Fig 1: Flow chart showing the pathway of whey production



The curd obtained above is transformed into cheese. A number of microbial and chemical phenomenons take place during ageing process. Thousands of techniques and variations are known to us by virtue of which various flavors develop. The ageing process requires a period of 2 weeks to 6 months based on the technique followed. But obtaining whey which is the pioneer compound for formation of novel products is rather a simple process. Moreover the so called art portion of cheese making is transformed into science when we are dealing with whey.

Medicinal value of whey in diseases

A disease is defined as an abnormal condition which affects the body of an organism. It is often associated with specific symptoms and signs. It may be caused by external factors like entry and survival of microorganisms or it may be caused by internal dysfunctions. In humans, "disease" is often used more broadly to refer to any condition that causes pain, dysfunction, distress and some time death. It is also caused due to oxidative stress and by nutrition depletion. Whey protein has been surveyed and found suitable against various diseases. Its medicinal value against a number of diseases has been discussed.

Cancer

Cancer remains an important health problem (Legge et al., 2010). Epidemiological and experimental studies have suggested that dietary milk products have an inhibitory effect on the development of tumors. Elevated glutathione concentration was reported in a number of tissues by whey supplementation (Bounous et al., 1991). Several experiments have demonstrated that glutathione levels is increased due to whey intake, in addition to this the intake of whey protein in diet promoted proliferation of activities of T cytotoxic cells, T helper cells, natural killer cells, increased splenic lymphocyte proliferation and process of phagocytosis. Many animal studies have examined the effects of whey and its immune-enhancing components, including lactoferrin and beta-lactoglobulin (Tsuda et al. 1998, Yoo et al. 1998, Tsuda et al. 2000, Hakkak et al. 2000, Hakkak et al. 2001, Kuhara et al. 2000). Activity of lectoferrin is marked by induction of apoptosis, inhibition of angiogenesis, and modulation of carcinogen metabolizing enzymes (Parodi, 2007). Among the different cellular mechanisms present to protect the cell, the GSH antioxidant system is ranked very high. In this context the use of whey protein strengthens GSH antioxidant system as shown in various animal studies. This occurs due to increased glutathione levels in concerned tissues. It is considered that oxygen radical generation is amongst one cause of carcinogenesis. Hence the carcinogen detoxification process of GSH is very important in suppressing carcinogenesis caused by various reasons (Bounous, 2000).

HIV

HIV infection is pandemic and anti-retroviral medication is not readily available (Feller et al., 2010). These infections are also related with decreased GSH levels. Whey protein diet has shown to increase the glutathione levels. This shows that whey supplementation can decrease the induction of co-infections (Moreno, 2006). Looking from another prospective, the HIV infection usually involves oxidant burden and deficiency of glutathione. The amino acid called cysteine present in whey supplies free thiol group for GSH synthesis. Thus this approach suggests different strategies to supplement cysteine supply to increase levels of glutathione in HIV-infected persons. In glutathione-deficient patients with advanced HIV-infection, short-term oral supplementation with whey proteins increased plasma glutathione levels (Micke et al., 2001). Patients maintaining proper caloric intake and whey protein supplementation showed increase in body weight and increase in GSH content of the mononuclear cells towards the optimal levels. Based on the above findings Bounous suggested that these findings can serve as a basis for an elaborate clinical trial (Bounous et al., 1993).

Effects of whey peptides in cardiovascular disease

Cardiovascular disease is becoming an important public health problem among Asian. Chinese and Indian women have very high rates and mortality from stroke. Stroke is also high in central Asian and Japanese women (Hu and Yu, 2010). Whey protein was reported to reduce the systolic and diastolic blood pressure. Low-density lipoprotein cholesterol and high-sensitivity C-reactive protein were significantly improved by whey intake. Whey-derived peptides might be a viable treatment option for prehypertensive and/or stage 1 hypertensive populations (Pins and Keenan, 2006).

Hepatitis

Acute viral hepatitis has recently become a major public health problem (Jung and Kim, 2009).The supplementation of whey protein demonstrated variable effects in patients infected with hepatitis B or C. Initially it was found that bovine lactoferrin prevented hepatitis C virus [HCV] infection *invitro* in a human hepatocyte cell line (Ikeda et al., 1998). These results prompted further clinical trials. However these trials left many unanswered questions for future studies regarding whey supplementation and HCV. This also includes optimum dose, duration and the potential effects of combining supplementation with conventional treatments such as interferon therapy (Marshall, 2004).

Blood pressure

Hypertension is an important risk factor for a number of cardiovascular diseases in many developing countries (Bosu, 2010). Whey proteins are precursors of some inhibitory peptide named lactokinins (Hartmann and Meisel, 2007) which have antihypertensive and anti-obesogenic properties. Lactorphin (Meisel, 2004), one of the important whey derived peptide affects adipocyte lipogenesis due to its inhibitory activity. A decrease in food intake due to this was also explained (Pupovac and Anderson, 2002, Froetschel et al. 2001).

Inflammatory response

The localized tissue response to any injury or trauma which involves any swelling, pain or redness is said to be an inflammatory

response. This response includes both localized and systemic effects, consists of altered pattern of blood flow, an influx of phagocytic and other immune cells, removal of foreign antigen and healing of damaged tissue. Unlikely to the effects of casein, the whey protein helps in reduction of inflammatory cytokines [IL-1 and IL-6], AST, ALT and LD (Kume et al., 2006). Hence the effects of whey protein on hypertension can be expressed by its affect on inflammation.

Role of whey protein in human health

Global climate change will have a wide range of health impacts. Public health problems caused by infectious diseases and by environmental contamination are a growing concern worldwide. Human health is mainly dependent on the food intake. In addition to this, factors like lifestyle, genetics, gender also affect the human health. Good food is essential for maintaining sound health. The importance of whey protein in human health was also reviewed.

Sports performance

Different proteins yield different patterns of amino acid appearance into the systemic circulation. Whey protein, result in a relatively rapid delivery of amino acids to peripheral tissues. Post exercise consumption of whey protein was also recommended (Dangin et al. 2003). Moreover various whey and whey-derived bioactive compounds have been studied for their ability to enhance general health and well being (Shah, 2000, Cross and Gill, 2000). Recent studies demonstrated that whey proteins and their constituent amino acids efficiently promote protein synthesis (Fouillet et al. 2002, Tipton et al. 1999).

Whey protein and satiety

When a comparison is made between whey protein and casein, then whey is classified as fast protein and casein is considered as slow protein. This classification is in accordance with their elucidated role on human food intake (Boirie et al., 1997). Looking from the hormonal prospective, whey proteins also have an effect on phenomenon of food intake and satiety. This is done through their role in release of satiety hormones. For example insulin which mediates both short term and long term regulations of food intake. The release of insulin is stimulated by whey. Thus along with glycemic responses, the concentration of insulin in plasma regulates satiety and decreases food intake (Samra et al., 2007). On the other hand, whey proteins are used as food supplements due to their unique characteristics like emulsifying, gelling, thickening, foaming and water binding capacity (Kinsella and Whitehead, 1989).

Whey protein in general health

Vitamin B12 is present in whey which is the sole source of indispensable nutrient for blood-formation and cell division in lacto-ovo-vegetarian nutrition (Barth and Behnke, 1997). It is also of a great importance in lactose intolerance and galactosemia (Barth and Behnke, 1997). Whey contains glutamine which serves as food for fast dividing cells and is very essential during metabolic stress conditions (Rosaneli et al. 2002). Whey proteins are now considered to be a next generation super-food as it can bind to specific minerals like iron, zinc, calcium, magnesium, potassium and sodium (Vegarud et al. 2000). The ingredients of whey are now commonly used to formulate feeding formulas for the new borns and also render great help to athletes and health conscious customers. There are various forms in which whey can be used like as tablets, sports mixes, protein bars, cookies etc. Whey has been shown to possess all essential amino acids and thus considered as high quality proteins (Hoffman and Falvo, 2004).

Whey components and adiposity

Obesity is a universal health problem of increasing prevalence and represents a major public health concern (Singh et al., 2010). Excess weight and adiposity has been also reported in children (Esquivel and González, 2010). Recent studies have shown that whey offer a nutritional advantage for achieving a desirable body composition. These studies show that calcium and mineral mix provided by dairy products decreases deposition of body fat and promotes weight and fat loss in conditions of energy restriction (Zemel et al. 2000, Zemel, 2003, Zemel et al., 2002, Shi et al. 2001, Lin et al., 2000). This suggested that whey supplements might facilitate achieving a favorable body weight.

Biotechnological prospective

Different strategies for the utilization of whey have been developed over the past few years. About half of the whey produced nowadays is not a pollutant but a resource. About 50% of total world cheese-whey production is now treated and transformed into various food products, of which, about 45% has been reported to be used directly in liquid form, 30% in the form of powdered cheese whey, 15% as lactose, and the rest as cheese whey-protein concentrates (Marwaha and Kennedy, 1988).

The treatment of whey by fermenting lactose to ethanol has received wide attention in the recent times. Several distilleries producing ethanol from whey are in commercial operation in countries like Ireland, USA and New Zealand (Mawson, 1994). By recombinant DNA techniques, Sacchomyces cerevisiae could be developed directly on cheese whey producing high yields of ethanol or other commercially useful fermentation products (Porro et al., 1992). Microbial biomass has been produced commercially from whey since the 1940s. Industrial microbial biomass production from cheese whey for use as food started in France at Fromageries Le Bel around 1958 (Moulin and Galzy, 1984). In addition to the above, extensive research has been, and continues to be, conducted on profitable byproducts that can be obtained from cheese whey. The areas for the investigation comprises of several organic acids with food uses (acetic, propionic, lactic, lacto bionic, citric, gluconic and itaconic), vitamins (B_{12} and B_2, or cobalamins and riboflavin, respectively), and amino acids (glutamic, lysine, threonine) can be obtained from whey by different microorganisms and processes (Hobman, 1984, Blanc and Goma, 1989, Nielsen et al. 1990, Fairbrother et al. 1991, Roukas and Kotzekidou, 1991, Zayed and Zahran, 1991, Chiarini et al. 1992, Colomban et al. 1993, Fournier et al. 1993, Norton et al., 1994). The use of whey protein was demonstrated in beverage preparation also (Sinha et al, 2007).

Conclusion

This article explained the composition and production of whey. It also explained its significance role in human diseases particularly in cancer, HIV, hepatitis, cardiovascular disease and also in hypertension. The article explained its role in sport and general health. Innovation is important for life science and economy, but the value of innovation for public health depends on its impact on promoting health. It is the requirement of present time to explore the potential of whey protein and also its protective effect against different diseases in human. Molecular level study is required to explore whey to improve the quality of dairy products.

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