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EMERGING HEALTH BENEFITS OF DAIRY PROTEINS

SUMMARY

Cow's milk is an excellent source of high quality protein, providing all of the essential amino acids needed by humans. Emerging scientific findings indicate that milk proteins – casein and whey and their bioactive peptides and amino acids – provide a variety of health benefits not previously recognized. As a result of this new knowledge and advances in technologies to isolate healthful protein components from milk, dairy proteins are being incorporated as value-added ingredients in a variety of foods and beverages.

Dairy protein, by virtue of being a high quality protein with an amino acid composition similar to that of the human body and a rich source of branched chain amino acids, especially leucine, helps support normal maintenance and growth of muscle. Adequate body muscle is important not only for physical performance/athletics, but also for overall health and prevention of disease. Data from independent human intervention trials have been remarkably consistent in demonstrating the ability of dairy protein (in the form of whey, casein, fluid milk, or extracted milk protein) to stimulate whole body and muscle protein synthesis under resting and exercise conditions. Findings supporting the beneficial role of dairy proteins in building and maintaining muscle mass lay the foundation for structure-function label claims on foods and beverages containing milk-derived proteins.

Dairy proteins, because of their high content of leucine, are of interest in weight control. Leucine has a unique role in increasing fat loss and promoting lean muscle tissue, as well as regulating blood glucose levels. Also, dairy proteins may contribute to satiety and suppress food intake, at least in the short-term. Because of their ability to help promote a desirable body composition (i.e., increase lean muscle mass) and to improve recovery from exercise, intake of dairy protein is important for physically active people seeking to optimize performance.

Studies in spontaneously hypertensive rats and some investigations in humans demonstrate that dairy protein reduces high blood pressure. A hypotensive effect of both whey and casein hydrolysates has been shown in hypertensive adults. Casein and whey are rich sources of angiotensin converting enzyme inhibitory peptides which have been shown to reduce blood pressure. The antihypertensive effect of dairy proteins has led to the manufacturing and marketing of dairy protein-enhanced beverages to reduce blood pressure.

In addition to the above emerging roles for dairy proteins, studies suggest their potential beneficial effect in bone and dental health and protection against toxins, bacteria, and viruses. As dairy proteins' role in health continues to grow, consumers can expect to see an increasing number of products on the market aimed at promoting the functional ingredient potential of milk protein.

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INTRODUCTION

The high protein diet craze has fueled an interest in high protein food products and has created a market for protein-enriched foods and beverages. Increasing knowledge of the nutritional and health benefits of dairy proteins – casein and whey and their bioactive peptides and amino acids – is leading to recognition of their potential as value-added ingredients in many functional foods and beverages, not only for weight management, but also for other health benefits (1,2). New and improved protein fractionation methods enable food processors to isolate healthful protein components from milk and incorporate these ingredients into various foods and beverages, including products for sports nutrition and weight management (3-5).

Cow's milk is an excellent source of high quality protein, providing varying amounts of all of the essential amino acids that humans cannot synthesize and in proportions resembling amino acid requirements (6,7). Cow's milk contains about 3.5% protein, of which 80% is casein and 20% is whey (8). Caseins include four subclasses: alpha-, beta-, gamma-, and kappa-casein. Whey protein, which is more heterogeneous than casein, includes several different proteins such as beta-lactoglobulin, alpha-lactalbumin, immunoglobulins, bovine serum albumin, lactoferrin, and lactoperoxidase, as well as glycomacropeptide, a casein-derived peptide (5,8). Each of these dairy proteins and peptides is emerging as having unique biological properties.

The importance of whey protein as a value-added ingredient with health and nutrition benefits was recently addressed at the 4th International Whey Conference held in Chicago, IL in September 2005 (2). Internationally recognized experts ranging from dairy researchers and processors to leading health and nutrition specialists presented new research findings and information related to the nutritional, health, and functional properties of whey protein, as well as their commercial applications. With respect to nutrition and health, researchers examined the role of whey protein in muscle metabolism and body composition, weight management and satiety, and immune health and chronic diseases, among other potential health benefits (2).

Research demonstrating dairy proteins' role in building and maintaining muscle mass lays the foundation for structure-function label claims on foods and beverages containing milk-derived proteins.

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This *Digest* reviews emerging research presented at the 4th International Whey Conference and from the published scientific literature related to selected health benefits of dairy proteins. Specifically, the role of dairy-derived proteins in muscle protein synthesis and accretion, weight management, physical/sports performance, and blood pressure control, as well as other biological functions are discussed. Also mentioned are some practical applications of this knowledge. For additional information on the health benefits of dairy proteins, readers are referred to several reviews/reports (4,5, 9-15) and to the proceedings of recent conferences (1,2).

EMERGING HEALTH BENEFITS

Muscle Protein Synthesis and Accretion. The importance of enhancing muscle mass, strength, and metabolic functions for athletes has long been recognized. However, it is now becoming appreciated that increasing and/or maintaining muscle mass is important for all individuals to help prevent disorders such as obesity, diabetes, osteoporosis, and sarcopenia (i.e., loss of muscle mass with aging) (2a). Individuals with limited muscle mass reserves respond poorly to stress, and in older adults loss of muscle mass or strength increases frailty and risk of falls as well as impairs the ability to perform daily activities (2a). Although resistance exercise stimulates muscle protein synthesis, it alone is insufficient to build muscle. Rather, the interaction of resistance exercise and nutritional intake results in muscle anabolism.

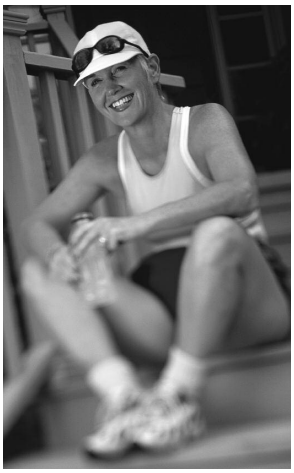
Dairy proteins, specifically casein and whey, are high quality protein sources that provide all the essential amino acids, and in particular the branched chain amino acid leucine, which has been shown to specifically stimulate the synthesis of new muscle protein (11,16,17). Additionally, dairy protein (in the form of whey, casein, fluid milk, or extracted milk protein) has been shown to directly stimulate whole body and/or muscle protein synthesis in humans (18-29). This finding is not surprising given

the high quality of dairy protein and the similarity of its amino acid composition to that of total body protein (30).

Several studies demonstrate the superiority of dairy protein as compared to soy protein in stimulating muscle protein synthesis (21-24). A randomized trial of 19 healthy adults fed either milk protein or soy protein mixed with sucrose found that milk protein stimulated protein anabolism in both the splanchnic (visceral) and muscle compartments and was preferentially taken up by the muscle as compared to soy protein (22). Similarly, in another randomized intervention study in 20 healthy adults on an adequate protein diet and under non-exercised conditions, milk protein resulted in a greater stimulation of whole body protein synthesis than soy protein (21). Other investigations demonstrate that whole body protein synthesis is greater after casein than soy and that soy protein is degraded to urea to a greater extent than casein (23,24). These studies show that under resting conditions dairy protein results in a greater protein synthesis in the body than soy. However, further research is needed to determine whether these proteins differ in their effect on muscle accretion.

The benefits of dairy protein on muscle protein synthesis during recovery after resistance exercise have also been demonstrated (2b,25-29). In a study comparing acute consumption of casein to whey protein under exercised conditions, both dairy proteins similarly stimulated muscle protein synthesis compared to a control (26). In another short-term study, milk intake stimulated nitrogen uptake, a predictor of muscle protein synthesis, to a greater extent than soy after exercise in young men (27). In a long-term (12 weeks) follow-up study, consumption of milk plus exercise resulted in a trend towards greater muscle fiber size than soy (27). Findings from other long-term studies (10 weeks) in adults suggest a trend towards greater gains in lean body mass with dairy protein (whey, milk) intake after a resistance exercise training program as compared to consumption of a carbohydrate beverage alone (28,29).

The above scientific findings from human intervention trials lay the foundation for structure-function claims associating dairy protein with building and maintaining muscle mass. Structure-function claims on food and beverage labels describe the role of a nutrient or dietary ingredient intended to affect normal structure or function in humans (31). Examples of some potential structure-function claims related to dairy proteins and muscle mass include the following: "Dairy protein (whey and casein) helps support normal maintenance and growth of muscle" or "Dairy protein (whey and casein) provides essential amino acids that augment protein synthesis and new muscle growth during recovery from intense resistance exercise."



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Dairy proteins may have a beneficial impact on body weight by their effect on lean muscle mass and possibly satiety/ food intake.

Weight Management. Considerable evidence has recently accumulated to support a beneficial role for dairy products in weight management (32). Findings that dairy is more effective than calcium in inhibiting weight and fat gain and accelerating fat loss during energy restriction suggest that other components in dairy foods may be involved. The augmented effect of dairy products compared to supplemental calcium is believed to reside in part in the whey protein fraction (32).

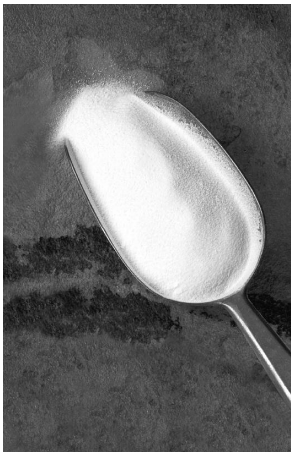
Short-term studies in adults demonstrate that diets elevated in high quality protein, including dairy protein, and low in carbohydrate have beneficial effects on body weight (17, 33-35). Emerging research indicates that the metabolic advantages of protein-rich diets during energy restriction include sparing of lean body mass loss, enhancing glycemic control, and increasing thermogenesis and satiety (17,33-35). That is, protein-rich diets reduce loss of lean tissue and increase loss of body fat during weight reduction. Since muscle burns more fuel, a higher proportion of lean tissue will help achieve greater long-term weight loss and maintenance of weight loss. A long-term study (16 weeks) in adult women showed that dietary protein and exercise had an additive effect on improving body composition during weight loss (36). The merits of higher protein diets for weight loss are attributed to increased levels of branched chain amino acids, especially leucine (17). Dairy proteins, particularly whey protein, are a particularly rich source of leucine and other branched chain amino acids (11). Leucine has unique roles in the

regulation of muscle protein synthesis and glycemic control. For example, leucine stimulates recovery of muscle protein synthesis during energy restriction or after endurance exercise (17,34). Thus, leucine helps minimize muscle wasting. Leucine also appears to modulate glucose use by skeletal muscle and provides a stable glucose environment with low insulin responses during energy restriction (17,34). The impact of these regulatory roles of leucine and branched chain amino acids is proportional to their availability and dietary intake (33).

Dairy proteins may also influence body weight by their impact on satiety and food intake (2c,37,38). However, the effect of the milk protein source on short-term satiety and food intake in humans is mixed. Higher subjective satiety and lower food intake at a buffet meal 90 minutes later was reported in subjects who consumed drinks containing whey compared to a beverage with an equivalent amount of casein (39). The increased satiety response of whey was attributed to the increase in plasma amino acids and secretion of cholecystokinin and glucagon-like peptide 1, which reduce gastric emptying. In another investigation, intake of commercial preparations of whey and soy protein, but not egg protein, suppressed food intake from a pizza meal consumed one to two hours later (38). In another investigation reported by Anderson and colleagues (2c), food intake was similarly decreased by casein, whey, and complete milk protein drinks at 90 minutes, but at 150 minutes, casein suppressed food intake more than whey. In a recent study in 19 overweight men, acute appetite and energy intake were equally reduced after consumption of lactose, casein, or whey compared with glucose (40). This finding was consistent with differences in plasma levels of ghrelin (a hunger hormone). Further research is needed to clarify the effect of specific milk proteins on satiety and food intake.

The benefits of whey protein in weight management have been demonstrated in experimental animals and humans.

Dairy proteins (casein and whey) provide essential amino acids that help augment protein synthesis and new muscle growth during recovery from exercise.



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Studies in experimental animals have shown that whey protein positively affects lean mass accretion and may reduce body fat mass (41,42). USDA researchers reported preliminary findings from a double-blind, randomized clinical trial involving 90 overweight or obese adults showing that those who consumed supplemental whey protein for six months weighed less and had less body fat compared to a control group receiving a carbohydrate supplement (43).

Physical/Sports Performance. To maximize physical performance, physically active people desire a high proportion of muscle to body fat mass (11). Dairy proteins (whey and casein) provide essential amino acids, particularly branched chain amino acids such as leucine, that help attenuate the breakdown of muscle proteins during exercise and promote protein synthesis in skeletal muscle following exercise (2b,2d,11,18,26-29,43). Branched chain amino acids are an energy source during endurance exercise and may also help speed muscle recovery from exercise (11,43,44).

Phillips (2b) proposes that a 1:1 blend of whey to casein may be optimal to stimulate muscle protein anabolism following resistance exercise given the ability of whey protein (i.e., characterized as a "fast" protein because it results in a rapid increase in blood amino acids) to stimulate muscle protein synthesis and that of casein (i.e., a "slow" protein) to suppress the breakdown of muscle protein (18). Studies have shown that intake of milk or a whey protein beverage promotes greater gains in muscle mass or lean body mass following resistance training than carbohydrate alone (28,29). A recent study in healthy young volunteers found that intake of protein in the form of food, specifically milk, following resistance training increased uptake of the amino acids, phenylalanine and threonine, which is representative of net muscle protein synthesis (45). Dietary protein also stimulates insulin levels, improving the uptake of glucose into glycogen-depleted muscles (2d). A study in exercise-trained rats found

that a diet based on whey protein significantly increased the glycogen content in liver and skeletal muscle (46). Findings from these studies support the benefits of dairy proteins for physically active individuals.

Blood Pressure Control. Milk proteins may reduce high blood pressure, a controllable risk factor for cardiovascular disease (2e,4,9,47-49). Casein and whey proteins are rich sources of angiotensin converting enzyme (ACE) inhibitory peptides. ACE converts the inactive angiotensin I hormone into angiotensin II, which constricts vascular smooth muscle, thereby increasing blood pressure (47). Inhibiting ACE lowers blood pressure. Studies in spontaneously hypertensive rats have demonstrated that potent ACE inhibitory peptides hydrolyzed from individual caseins and whey proteins reduce systolic blood pressure from 2 to 34 mm Hg (9,47).

Human studies, mostly short-term, have investigated the anti-hypertensive effect of different milk protein hydrolysates in individuals with high blood pressure (47-49). In a 6-week randomized controlled study in 30 mildly hypertensive adults, a hydrolyzed whey protein isolate significantly reduced systolic and diastolic blood pressure compared with a nonhydrolyzed whey protein isolate control (2e,47). In another placebo controlled randomized trial in 10 hypertensive adults, a single dose of a casein hydrolysate called C12 peptide significantly reduced systolic and diastolic blood pressure (48). Also, intake of two tripeptides (Valine-Proline-Proline and Isoleucine-Proline-Proline) with ACE inhibitory activity reduced systolic blood pressure in a dose-dependent manner in a 6-week single blind controlled study in 131 adults with high-normal blood pressure (49).

Emerging scientific evidence supporting the blood pressure-lowering effect of milk-derived peptides is increasing the availability of a number of food products in the form of dairy beverages or as milk protein hydrolysates (e.g., BioZate, a whey protein hydrolysate in the U.S.; C12 peptide, a casein hydrolysate in the Netherlands; and casein DP, a casein hydrolysate in Japan) (47). Although more long-term clinical trials are necessary to confirm their efficacy in lowering blood pressure, these milk-derived proteins could potentially serve as a viable treatment option for individuals with or at risk of hypertension.

Emerging scientific evidence indicates that dairy proteins and their bioactive peptides lower elevated blood pressure, support bone and dental health, and provide protection against toxins, bacteria, and viruses.

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Other Health Benefits. In addition to the above, dairy proteins may confer several other health benefits. Cow's milk has been shown to contain bioactive proteins with bone-protective properties (50-55). In vitro, experimental animal, and human studies demonstrate a bone-strengthening effect of milk basic protein, a component of whey protein (50,51). Lactoferrin, another whey protein, is identified as a novel bone growth factor with potential therapeutic use in the treatment of osteoporosis (52,53).

Lactoferrin, as well as other milk-derived bioactive peptides, also has a beneficial role in dental health by inhibiting cariogenic, plaque-forming bacteria and tooth enamel demineralization and promoting remineralization of tooth enamel (56-58). Caseinphosphopeptide (CPP) and glycomacropeptide (GMP) have been patented for use in common personal hygiene products (e.g., toothpaste, mouth rinses) to prevent dental caries (56). Adding casein phosphopeptide-amorphous calcium phosphate to sugar-free gum (57) or sports drinks (58) has been shown to help prevent dental caries. A biologically active extract of bovine whey proteins formulated into a mouthwash has been clinically shown to mitigate mouth ulcerations in humans undergoing cancer chemotherapy (59). Mouth ulcerations, or oral mucositis, is a common complication in cancer patients that limits both the dosage and duration of chemotherapy.

Dairy proteins contain several components such as immunoglobulins, lactoferrin, growth factors, and amino acids (necessary to support glutathione production) that provide protection against toxins, bacteria, and viruses (2f,5,60-64). Lactoferrin, because of its iron-binding properties, can enhance

the immune response and reduce inflammation (2f,61). For example, lactoferrin has been demonstrated to increase immobilization-stress induced immune responses in mice and in patients with multiple sclerosis (2f). Other studies have shown that lactoferrin attenuates pneumonia in influenza virus-infected mice (62); that GMP may play a role in the management of patients with inflammatory bowel disease or some liver diseases (63); and that whey protein concentrate reduces rotavirus-induced diarrhea in mice (64). Some recent studies indicate that milk proteins, by stimulating insulin release, may be beneficial for type 2 diabetic patients (65,66).

CONCLUSION

It is now recognized that foods can have health-promoting properties that extend beyond their nutritional value (67). This, along with increasing research data supporting the role of dairy proteins in health promotion and disease prevention, is expected to substantially expand the use of dairy proteins as value-added ingredients in a variety of foods and beverages. D

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