Bio-Active Peptides [BAP's]

Their Role in Protein Synthesis and Human Performance Enhancement Related to Recovery and Lean Body Mass Gains

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*There is an abundance of scientific and anecdotal evidence that suggests protein is useful for a wide array of beneficial performance enhancements, but a new emergence of designer supplementation, named **"Bio-Active Peptides"**—isolated sub-fractions of protein molecules containing high concentrations of growth factors—could become the new natural compound of choice for athletes in search of enhanced recovery, improved strength, and lean body mass development. To follow is a scientific summary of what bio-active peptides are, along with how they work, what they have to offer us, and how to use them for optimal performance enhancement.*

Origins of Bio-Active Protein Peptides

In the late 1800's, the Polish researcher Stanislaus Bondzynski discovered natural "bio-active peptides" in the body but did not realize at that time the true power they possessed on function, disease prevention, and their possible roles in addressing cancer. Although published in scientific journals of the time, his findings were ignored by all but a few. Over the years, 1,200-plus unique bio-actives have been identified to be present within plant and animal proteins. Today, bio-active peptides are a big-ticket item for drug companies searching for new ways to improve health, recovery, stunted growth, and immune function. Those peptides, such as insulin and growth hormone, for example, have changed the face of medicine over the last several decades; however, their use in athletics is prohibited. For those in the dietary supplement world, on the other hand, bio-active peptides represent a new breed of supplements that may improve performance, reduce time to recovery due to inflammation (swelling and soreness) and immune-function, post-exercise recovery, and most excitingly, increase the efficiency of muscle-mass development.

There is little doubt bio-actives peptides are a major find and a potential breakthrough as a natural nontoxic treatment in an array of human ailments. Many companies have begun investigating additional benefits beyond treatment and prevention of disease, and some have produced products that may aid not only in recovery but also reduction of inflammation and pain management. Additional research and testing has now begun on the potential powerful benefits to those engaged in exercise and athletics. A handful of companies have produced commercially available products that contain lactoferrin, immunoglobins, and some other bio-actives, and they have even marketed them in the performance arena. However, only one nutritional company is producing a specific supplement engineered toward improving muscle protein synthesis and recovery, with *additional* bio-actives present, as it relates to resistance training, sports performance, and enhancement of lean body mass. It is patent-pending (USPTO No. 50925-00001) and found under the trade name Bio-Pro Bio-Active Peptides™.

What Are Bio-Active Peptides?

Bio-active peptides are specific protein fragments beneficial to various physiological systems within the body, such as cardiovascular, digestive, immune, and nervous systems, thereby positively influencing health. The beneficial health effects may be classified as anti-microbial, anti-oxidative, anti-thrombotic, anti-hypertensive, anti-microbial, and immune-modulatory [24]. Additionally, bio-active peptides play a role in protein metabolism and protein synthesis and thus have an effect on the musculoskeletal system.

Diet is known to play an important role in the body's defense mechanism, and research concerning the role of orally delivered functional peptides on the immune system is promising. The two main activities being studied are the immunomodulatory (stimulation of immune system) and antimicrobial (inhibition of microorganisms) effects of bio-active peptides. Casein, whey, and other protein-derived peptides display an immunomodulatory role when consumed exogenously. Immunomodulating peptides have been found to stimulate the proliferation of human lymphocytes, the phagocytic activities of macrophages and antibody synthesis. Also, it has been suggested that immunomodulatory milk peptides may alleviate allergic reactions in humans and enhance mucosal immunity in the gastrointestinal tract [24]. Improving immune function may have a positive transfer effect to the athletic world in that it would reduce time to recovery, control cell inflammation, and eliminate or reduce possible "downtime" brought on by an athlete's inability to train due to an impaired immune system or general sickness, thus increasing his or her ability to continue to exercise at higher levels or for longer durations.

On the cutting-edge of sports supplement science is the notion of fractioning various milk protein derivatives down to the peptides responsible for muscle-protein synthesis and the transcription, proliferation, and development of muscle cells and muscle function. In much the same fashion as immune-stimulating bio-active peptides have been derived, the focus, for those interested in improving performance, has shifted to examining the peptide chains responsible for signaling activity and delivering information that allows muscle to replicate and rebuild. While the data is highly supportive in animal models, performance and training studies in humans has been limited. However, several studies have indicated that colostrum, which is **naturally very high in bio-active peptides, is superior to whey proteins for post-exercise recovery, improvement in performance, and development of lean body mass over a defined training period** [2, 9, 11, 22].

How Bio-Active Peptides Work in the Body

Bio-active peptides display a variety of activities as a result of their specific amino-acid composition and sequence. There are many bio-active peptides in the body, and the size of active sequences may vary from two (di-peptide) to 20 amino-acid residues (oligo-peptide). Many peptides are known to possess multifunctional properties [30]. For example, ß-casein displays immune-stimulatory, opioid, and angiotensin I converting enzyme (ACE)-inhibitory activities. This sequence has been defined as a "strategic zone" [31]. These peptides are typically protected from degradation because of its high hydrophobicity and the presence of proline residues. As a result, the peptides are also referred to as proline-rich polypeptides. In the case of milk-derived peptides, other examples of the multifunctionality of these bio-active peptides include the αs1-casein fraction showing immunomodulatory and ACE-inhibitory activity, the opioid peptides α- and ß-lactorphin also exhibiting ACE-inhibitory activity, and the calcium-binding phosphopeptides which possess immune-modulatory properties [24].

Some bio-active peptides act as signaling molecules, while others perform direct functions as their hormone form would indicate. In addition to their powerful immune-modulatory responses, bio-active peptides perform functions on the cardiovascular, nervous, digestive, and musculature systems. Though they can be broken down from larger proteins when consumed, via milk and other sources [37], it is more advantageous if the whole protein sources are able to be hydrolyzed down to their fractioned bio-active peptide, and then they are able to fully express and exhibit their characteristics [37] when needed by the body. Often these smaller fractioned components are unable to be utilized by the body during the process of breaking down normal whole proteins, which may destroy the finer constituents before they are able to provide their benefit. However, when directly consumed, as fractioned bio-active peptide form (via a specific engineered process) due to their extracted form, they are able to be utilized and perform their direct function on the target tissues.

Where Bio-Active Protein Peptides Are Derived

Bio-active peptides can be derived from plant or animal proteins. More recently, a number of bio-active peptides are derived specifically from certain milk proteins. Casein and whey are the two main protein groups in milk. Casein proteins comprise about 80% of the total protein content in bovine milk and are divided into α-, ß- and κ-caseins. In regards to whey protein, it is composed of ß-lactoglobulin, α-lactalbumin, immunoglobulins (IgG's), glycomacropeptides, bovine serum albumin, and minor proteins such as lactoperoxidase, lysozyme, and lactoferrin [27]. Each of the protein sub-fractions found in casein or whey has its own unique biological properties. Milk proteins can be degraded into numerous peptide fragments and liberated by enzymatic proteolysis during gastrointestinal digestion to produce a number of bio-active peptides.

Colostrum is a superior source of bio-actives, primarily because it is naturally higher in the important bio-active peptides than other sources of protein, even whey. Colostrum is the pre-milk fluid produced from the mother's mammary glands during the first few days after birth. Colostrum is a rich source of antibodies, growth factors, and nutrients for the suckling neonate and may provide passive immunity to the newborn against various infectious microorganisms, particularly those that affect the gastrointestinal tract, and helps to instigate the growth and development of the newborn. Colostrum is also rich in immune, growth, and antimicrobial factors such as insulin-like growth factors 1 and 2 (IgF-1, -2), transforming growth factor beta (TGF-ß), epidermal growth factor (EGF), fibroblast growth factor, platelet-derived growth factor (PGF), immunoglobulins (IgA), cytokines, lactoferrin, lysozyme, and proline-rich polypeptides (PRP's). In addition to hormones such as growth hormone, colostrum also contains gonadotrophin-releasing hormone, luteinizing hormone-releasing hormone, and glucocorticoids, which are all highly important in promoting tissue growth and development in neonates.

The bio-active peptides and growth factors particularly important to athletic performance are:

- **Insulin-like Growth Factor-1 (IGF-1)**
- **Proline-Rich Peptides (PRP's)**
- **Immunglobulines (IgA)**
- **Lactoferrin**
- **Fibroblast GF**

The proline-rich polypeptides (PRP's) are a vitally important component for colostrum. PRP's are small peptides that have a robust effect in initiating and balancing immune responses. There are five different proline-rich polypeptides (PRP 1-5). PRP 2 and 3 are most active, and PRP 2 is thought to contain active peptides that are used to modulate cytokine levels in the body, particularly interferon beta, which has anti-viral properties. PRP 3 modulates the interferon alpha levels in the body, which is involved in modulating the auto-immune responses. These peptides can act as molecular signalers which promote the growth and the differentiation of B-cells, and promote leukocytosis [proliferation of leukocytes (white blood cells)] [29]. In all, PRP's act as "air-traffic controllers," telling the various enzymes and hormones, via a signal, where and when to move about to get the specific activation required to carry out their needed functions.

What Does the Science Say About Colostrum?

The value of bovine colostrum supplementation in human adults is still under extensive study, and therefore, all of its benefits are not completely understood; however, initial research indicates positive effects in a number of physiological systems. For instance, colostrum supplementation is becoming increasingly popular in exercising individuals with the goal of augmenting exercise performance and enhancing lean body mass. Heavy, high-intensity anaerobic exercise or prolonged endurance exercise induces physiological stress and causes acute depression of many components of the immune system [34]. Within colostrum, the combined presence of IGF-1, TGF's, immunoglobulins, cytokines, lactoferrin, and lysozyme, in addition to hormones such as growth hormone, gonadotrophin-releasing hormone, and luteinizing hormone-releasing hormone, suggests bovine colostrum likely improves the function of the immune, gastrointestinal,

neuroendocrine, and skeletal muscle systems, as these are all parameters that may be compromised and are in greater need as a result of heavy, intensive resistance training. A review of studies investigating the influence of bovine supplementation on exercise performance discussed below suggests its effects to be most pronounced during periods of high-intensity training along with recovery from high-intensity training. While the mechanisms are still being examined, much of the improvement is likely due to the result of increased plasma growth factors (i.e., IGF-1) and improved intramuscular buffering capacity leading to increases in lean body mass and improvements in immune function (i.e., increases in salivary IgA).

Not all colostrums are the same. Proteins can be engineered to have much higher concentrations of various amino acids and peptides during the manufacturing process. For colostrum, there are two main elements that will help to derive specific peptide-rich components. The first is the point at which the colostrum is retrieved, and the second is the actual fractioning process to extract specific constituents. The earlier on after birth that colostrum is collected from the birthing cow, the more pure it is to begin with. Using a more pure form ensures a higher concentration of important bio-actives are available. Most colostrums are derived some 48 to 96 hours after birth; however, there are some higher grade forms of colostrum collected within the first 12 to 24 hours.

Colostrum *versus* Whey Protein: A Scientific Comparison

Initially, it was believed colostrum would only possess properties that would aid infants or immune-impaired or diseased people. It is now understood that specific collection and fractioning of colostrum could play a potentially powerful effect on athletic performance variables.

Bovine colostrum is a rich source of antibodies, growth factors, and nutrients that are homologous to those found in human colostrum but expressed in greater concentrations [40]. Bio-active peptide concentrations are greatest in the first milkings, but decrease over the subsequent three days [23]. Colostrum provides passive transfer of immunity to the newborn whose immune system is not fully developed at birth and a source of growth factors to contribute to the development of the digestive tract, cellular and musculature functions [3]. Colostrum is lower in fat, and the protein content is three to four times higher (up to 150 grams/liter compared to 30 to 40 grams per liter) than regular cow's milk. Unlike whey protein, immune-related factors such as immunoglobulins, cytokines, lactoferrin, and lysozymes are found in colostrum along with the vital growth factors, insulin-like growth factors 1 and 2 (IGF-1 and IGF-2), transforming growth factors (TGF's), epidermal growth factor, fibroblast growth factor, and platelet-derived growth factor. Of the growth factors contained in bovine colostrum, the most prevalent is IGF-1 with a circulating concentration of 7-67 nmol/l [38] while the concentration of normal milk is < 0.3 nmol/l [10]. In adult humans, the normal level of IGF-1 in circulation is approximately 7 nmol/l [20]. The other growth factors in colostrum, transforming growth factor (TGF-β), epidermal growth factor (EGF), and fibroblast growth factor are important because they all play a role in cell proliferation and repair [45].

Unlike whey protein, bovine colostrum also contains a number of hormones known to influence the hypothalamus, pituitary and adrenal glands, and gonadal function [15]. Specific hormones include growth hormone, gonadotrophin-releasing hormone, luteinizing hormone-releasing hormone, glucocorticoids, and possibly testosterone [43]. The function of these hormones in colostrum is not clear; however, it is postulated that they play a role in gastrointestinal development, immune system maturation, and musculature development of the neonate. Oligosaccharides and glycoproteins contained in bovine colostrum may provide an energy source [18] while α-1 acid glycoprotein may be an important modulator of inflammation [6].

Another important, yet commonly overlooked, contribution to the protein content of colostrum comes from immunoglobulins and the concentrations of IgG, IgM, and IgA, which are up to 100 times greater than the concentration found in normal milk [28]. IgG is able to enhance the cytotoxic activity of natural killer cells and phagocytosis by binding to macrophages and neutrophils [39]. Colostrum also contains a number of cytokines important in stimulating the calf immune system and also important messengers within the human immune system [39]. In addition to lactoferrin, lysozyme, proline-rich peptides, and hormones such as growth hormone, colostrum also contains gonadotrophin-releasing hormone, luteinizing hormone-releasing hormone, and

glucocorticoids, which are all highly important in promoting tissue growth and development. An additional feature of colostrum that helps differentiate its powerful effects from other proteins is the high concentration of proline-rich polypeptide (PRP's). These are small peptides that have a marked effect in initiating and balancing internal responses and cell signaling from the muscle nuclei. For instance, during exercise, when the immune system is compromised or the muscle cell is under stress, and cells are calling for help, the PRP's are a welcomed addition to help amplify the cell's signaling ability and thereby help improve the act of muscle-protein synthesis, repair, and recovery of muscle tissue.

Performance Enhancement

In a study by Kersick, et al. [22], comparing the effects of bovine colostrum or a blend of whey and casein along with creatine on body composition, muscular strength and endurance, and anaerobic performance during resistance training determined that *colostrum performed equally and better to that of the standard protein blend groups*. Physically active but non-resistance trained males participated in a standardized 12-week total body resistance training program. In a double-blind and randomized manner, subjects supplemented their diet with 60 grams/day of an isocaloric and isonitrogenous whey protein control, whey protein + bovine colostrum, whey protein + creatine, or bovine colostrum + creatine. Resistance training increased muscle strength and endurance and anaerobic sprint capacity equally in all groups; however, participants ingesting whey protein + creatine and bovine colostrum + creatine had greater increases in fat-free mass during training.

In yet another study, the effects of eight weeks of bovine colostrum supplementation, in conjunction with resistance training, on body composition and exercise performance in active men and women was determined by Antonio, et al. [2]. Participants were randomly assigned to a placebo (whey protein) and colostrum group (20 grams/day in powdered form). Each subject participated in aerobic and heavy-resistance training at least three times each week. Body composition, treadmill time to exhaustion, one-repetition maximum strength (bench press), and the total number of repetitions performed during one set to exhaustion at a submaximal load for the bench press (50% and 100% of body weight for women and men, respectively) were ascertained. **The whey protein group experienced a significant increase in body weight, whereas the *colostrum group experienced a significant increase in bone-free lean body mass***. This study indicated bovine colostrum supplementation at a dose of 20 grams/day in combination with resistance training for eight weeks increases bone-free lean body mass in active men and women.

In another study, researchers investigated the influence of low-dose bovine colostrum supplementation on exercise performance in male road cyclists over a 10-week training period that included five days of high-intensity training (HIT). One group was provided with 10 grams/day bovine colostrums, and the other group was provided with 10 grams/day whey protein as placebo. The effects of bovine colostrum during normal cycle training was unequivocal; at the end of the HIT period, compared to whey protein, the bovine colostrum group significantly improved 40-km time trial performance (while also maintaining time trial heart rate) and increased maximum oxygen consumption, while also preventing a decrease in ventilatory threshold. **The results from this study suggest low-dose bovine colostrum supplementation elicited improvements in 40-km time trial performance during the HIT period and maintained ventilatory threshold following five consecutive days of HIT [35], making it a worthy supplement for endurance training athletes.**

Another study was conducted analyzing the dose response of eight weeks of bovine colostrum supplementation on cycling performance [11] in which competitive cyclists were randomly divided into three groups and required to consume either 20 grams/day of bovine colostrum + 40 grams whey protein, 60 grams of bovine colostrum, or 60 grams of whey protein as a placebo. The performance measure was the time to complete a work-based time trial following a two-hour cycle at 65% VO2max. After supplementation, two subjects in the 20 g and 60 g groups completed the time trial significantly faster post supplement compared to pre supplement. Therefore**, bovine colostrum supplementation at 20 g or 60 grams/day for eight weeks provided a significant improvement in time trial performance in cyclists after a two-hour ride at 65% VO2max.**

Finally, a study was commissioned to examine the effects of whether bovine colostrum could reduce intestinal permeability induced by endurance exercise [5]. Healthy adult males completed eight weeks of running thrice weekly for 45 minutes at their lactate threshold while consuming 60 grams/day of bovine colostrum,

whey protein, or placebo. Intestinal permeability was assessed at baseline and after eight weeks by measuring the ratio of urinary lactulose and rhamnose excretion. After eight weeks, the lactulose/rhamnose ratio increased significantly more in the bovine colostrum group compared with whey protein and placebo. The increase in intestinal permeability with bovine colostrum may have been due to the induction of greater leakiness of tight junctions between enterocytes or by increasing macromolecular transport as it does in neonatal gut. While at first this may seem like a negative finding, it suggests certain peptides may be "leaking across" the digestive wall, and that could explain improved performances found in colostrum supplementation.

Immune and Recovery

In a study by Shing, et al., the influence of five weeks of low-dose bovine colostrum supplementation on selected immune variables in cyclists was determined [36]. Highly trained male road cyclists completed an initial 40-km time and were then randomly assigned to either 10 grams/day of bovine colostrum supplement or 10 grams/day of whey protein as a placebo. After five weeks of supplementation, the cyclists completed a second time trial and then completed five consecutive days of high-intensity training (HIT). **Compared with the whey protein group, bovine *colostrum supplementation significantly increased pre-exercise serum* soluble TNF Receptor 1, a type of cytokine that causes apoptis (cell death) receptor 1 during the HIT period. This increase is beneficial to improving protein synthesis and reducing inflammation.** Supplementation with bovine colostrum also suppressed the post-exercise decrease in cytotoxic/suppressor T cells during the HIT period and during the following week. Bovine colostrum supplementation prevented a post-exercise decrease in serum IgG concentration at the end of the HIT period. **These results suggest low-dose bovine colostrum supplementation modulates immune parameters during normal training and suggests time to recovery can be improved and overall performance increased.**

Another study was conducted to evaluate acute effects of bovine colostrum low-molecular weight fraction on selected aspects of innate immune function in healthy humans [21]. A placebo-controlled, double-blinded, randomized cross-over trial was conducted in which placebo or 150 mg bovine colostrum was given orally. Blood was drawn immediately before and at one and two hours after consumption. While not significantly different, a single dose of bovine colostrum, when compared to placebo, resulted in a rapid increase in phagocytic activity of monocytes at one hour. However, the increase in the activity of polymorphonuclear cells at one hour and two hours after consumption was significantly different. Additional significantly different observations included increased numbers of CD3(+) T cells, and a transient reduction in circulating CD3(-)CD56(+) natural killer (NK) cells at one hour, returning to normal levels at two hours after consumption. The relative increase of NK cells from one to two hours after consumption was not associated with an increase in CD69 or CD25 activation markers, suggesting new NK cells were mobilized into circulation. The increased phagocytic activity and rapid transient changes in NK cell numbers suggest that upon consumption, interaction of bovine colostrum with immune cells in the gut mucosa triggers immediate events with systemic consequences. **Again, these results suggest both recovery time and inflammation is reduced when using bovine colostrum as a supplement.**

In yet another study performed with the intent of determining the effects of two weeks of bovine colostrum supplementation at 20 grams/day on serum IGF-1 and salivary IgA in track and field athletes while also engaging in their training program. Female athletes were randomly assigned in a double-blind fashion to either a bovine colostrum or maltodextrose placebo group. After two weeks of bovine colostrum supplementation, significant increases in serum IGF-1 and salivary IgA compared to maltodextrose supplementation [33] were observed. It was concluded that a long-term supplementation of bovine colostrum increases serum IGF-I and saliva IgA concentration in athletes during training. These results have both positive and negative implications. For the athlete concerned with increasing protein synthesis, these findings suggest the increase in serum IGF-1 would indicate protein synthesis would be robust in functioning and provide a definite advantage for athletes looking to increase muscle size and strength as well as aiding in recovery. On the downside, these findings could suggest higher levels of IGF-1 may cause a positive drug test for the banned substance IGF-1 by certain athletic organizations.

However, in a study by Kuipers, et al., where athletes consumed 60g of bovine colostrum per day over a four-week period, ***no athletes tested positive on a drug test***. This suggests that while IGF-1 levels increase while using bovine colostrum-based products, the changes, while beneficial to performance and lean body mass improvements, do not raise IGF-1 higher than within normal, healthy ranges, to that of a banned substance level [26].

Other studies have been conducted and a full analysis suggests the question lies within the difference between a significant increase in IGF-1 levels (as reported during a study) versus an increase in IGF-1 to a level where it is beyond that of natural human production capabilities. As of now, it is safe to assume normal dosages of colostrum-based supplements, including those contained from bio-active peptides, are both safe and effective at increasing IGF-1 without pushing blood tests to a banned level. However, it should be stated, since all persons do not respond the same, athletes that are very concerned should consult a physician and/or submit to a blood test to determine their capacity for using such products.

Salivary IgA is a potential mucosal immune correlate of upper respiratory tract infection (URTI) status. As a result, a study was conducted to determine if bovine colostrum could be beneficial to athletes at increased risk of URTI. Male and female distance runners consumed either a bovine colostrum or placebo supplement for 12 weeks. Salivary IgA was significantly increased in the bovine colostrum group after 12 weeks. This significance was still apparent after adjusting for training volume and self-reporting of upper respiratory symptoms. This study has demonstrated increased salivary IgA levels in athletes following colostrum supplementation [9]. Anecdotal reports suggest bovine colostrum may prevent upper respiratory tract infection (URTI). However, there is a paucity of evidence to substantiate such claims. A study was conducted to examine whether bovine colostrum affected the incidence or duration of self-reported symptoms of URTI in adult males. Logbooks were examined containing self-reported symptoms of illness from previous studies which examined physiological effects of bovine colostrum. In these double-blind, placebo-controlled studies, participants had been randomly assigned to consume 60 grams/day of bovine colostrum or whey protein for eight weeks. Symptoms were coded using established criteria to identify those related to URTI. Since the incubation period for an URTI is up to five days, symptoms reported during the first week of supplementation (PRE-EXP) were analyzed separately to preclude those arising from infection prior to study commencement. During PRE-EXP, there was no difference in the proportion of subjects taking the different supplements who reported symptoms. During the subsequent seven weeks of the experimental period, a significantly lesser proportion of subjects taking bovine colostrum reported symptoms of URTI compared with those taking WP, but symptom duration did not differ. This study provided preliminary evidence that bovine colostrum may enhance resistance to the development of symptoms of URTI [4]. Since upper respiratory infections are both common and performance-inhibiting, being able to control this or reduce the possibility of occurrence, while not an immediate performance benefit, certainly merits supplementation for improving overall health and reducing downtime between training sessions.

Oral bovine colostrum supplementation has been shown to enhance immunity in human subjects. However, there is limited research on the use of bovine colostrum supplementation to counter exercise-induced immunodepression. Therefore, a study was conducted with the aim to determine if the effects of bovine colostrum supplementation on exercise-induced changes in innate immunity (neutrophil function and salivary lysozyme) in addition to salivary IgA. Apparently healthy, active men cycled for two hours at approximately 65% maximal oxygen uptake before and after four weeks of bovine colostrum or placebo supplementation with a daily dose of 20 grams/day. Results revealed exercise-induced significant decreases in neutrophil function (stimulated degranulation) and salivary lysozyme concentration and release that were more pronounced with bovine colostrum supplementation. **These results suggest four weeks of bovine colostrum supplementation limits the immunodepressive effects induced by acute, prolonged exercise [13]. Enhanced immunity reduces downtime, sickness, and improves recovery time, which can be substantial to improving overall volume of training.**

Role of Bio-Active Peptides in Assisting in Muscle-Mass Development

The combined presence of IGF-1, in addition to its ability to regulate the feedback and subsequent release of related hormones such as growth hormone, gonadotrophin-releasing hormone, and luteinizing hormone-releasing hormone, and possibly testosterone [1,42] suggests bovine colostrum improves functions of the neuroendocrine and neuromuscular systems, parameters that are up-regulated as a result of and stimulated by heavy, intensive exercise training. Studies investigating the influence of bovine colostrum supplementation on exercise performance suggest it may be most effective during periods of high-intensity training, as well as recovery from high-intensity training. The basis for this effectiveness is most likely a result of increased plasma IGF-1, improved intramuscular

buffering capacity, increases in lean body mass, and increases in salivary IgA.

Of the growth factors contained in bovine colostrum, the most prevalent is IGF-1. The IGF-1 in bovine colostrum has an amino acid sequence homologous to human IGF-1 [14]. IGF-1 has a pronounced anabolic effect on skeletal muscle [40], and it is directly associated with the regulatory feedback of growth hormone [25]. IGF-1 mediates the effects of growth hormone on muscle-protein synthesis [16], plays an important role in the regulation of metabolism [15], and can mimic most of the effects of growth hormone [12]. In addition, IGF-1 signals through the Akt/mTOR pathway, which has profound effects on the up-regulation of muscle-protein synthesis. This is an important point because bovine colostrum supplementation at a daily dose of 20 grams has been shown to significantly increase circulating levels of IGF-1 after only two weeks of supplementation [32].

Other growth factors in colostrum include TGF-β, epidermal growth factor, and fibroblast growth factor, which all play a role in cell proliferation and repair [14]. Growth hormone causes the liver to produce and release IGF-1 into circulation, thereby resulting in IGF-1 binding to its receptor and signaling through the Akt/mTOR pathway. Additionally, growth hormone can bind to its receptor and activate the ERK 1/2 signaling pathway involved in up-regulating the expression of various muscle specific genes to prepare them for translation into new muscle proteins [43].

How to Use Bio-Active Peptides; How Much and How Often?

It is now well established that bovine colostrum naturally contains a vast amount of bio-active peptides known to be associated with a number of physiological processes critically important to human health, performance, and lean body mass increases. Results from human studies have shown positive effects using a dose range from 10 grams/day [5,22,34,35]. The most conclusive studies have involved a dose of 12 – 20 grams/day [2,13,32]. However, when considering the use of bio-active peptides, which have been extracted from pure forms of high-grade bovine colostrums [as is the case from patent-pending Bio-Pro Bio-Active Peptides™], the dosages needed to impart a positive effect are much lower. These highly concentrated forms of bio-active peptides yielded from colostrum suggest much smaller doses would be required to receive the same and even more superior results than standard colostrum or even whey proteins. Through various pilot studies, and from anecdotal evidence, **the range of three to six grams/day appears to be the most beneficial**; however, more studies are needed to validate the optimal amounts of bio-active peptide usages.

Bio-active peptides should be supplemented at least twice daily and in situations with exercise resistance weight-training, athletic sports, or endurance events, where the individual might choose a nutrient-timing approach. Because of the half-life and usage of the bio-active growth factors within the body, dosages should be taken at least five to eight hours apart; with one usage in the first half of the day and another in the later part of the day. With that, it is theorized that at least one dose should be taken around the time of exercise, when the body is under the most stress and the need for protein is required by the muscle while synthesis is occurring. This means the daily doses of bio-active peptides can be ingested approximately 30 minutes prior to exercise, as part of a pre-workout nutrient approach; or the bio-active peptides can be taken during the exercise training period. Conversely, the bio-active peptides can be ingested immediately after exercise, as a post-workout recovery approach. Ideally, at least one dose is consumed around an exercise period; whereas the other/second dose would be consumed five to eight hours prior or later; for total of three to six grams consumed daily of bio-active peptides. [See side-bar commentary on optimal dosaging.]

Currently, it is theorized that dosages of bio-active peptides are body-weight dependent. As such, those persons weighing less than 90kg (200 lbs) may need to consume about three grams/day; and those persons weighing over 90 kg (200 lbs) may need to consume about six grams/day. However, it should be noted that there are many dependent variables that may control this prescribed dosage, such as stress, diet, volume, or intensity of exercise or training, and even the user's primary intended performance goal. In these instances, where demands are greater, such as where the user undergoes a higher volume or intensity of training or the intended performance goal is increased strength and/or increased lean body mass, the requirements for bio-active peptides may be greater (in the range of 9 – 15 grams/day). Additional studies are needed, and are currently underway, to help determine whether or not this theory is applicable. Nevertheless, research on these new bio-active peptides have demonstrated great efficacy at lower dosages, but at equivalent dosages, the results, while mostly anecdotal, have been very impressive.

An in-depth look at Bio-Pro Bio-Active Peptides, found inside Bio-Gro™: The only commercially available form of bio-active peptides within the nutritional supplements industry

Bio-Gro contains a number of specific growth factors that are isolated from colostrum and concentrated to provide a physiological effect that, once consumed, signals the body to amplify its natural protein synthesis process, helping users develop lean muscle and recover faster from intense workouts. The supplement does this by assisting a user's body to signal and accelerate the rate at which it processes the building and re-building of muscle tissue, called muscle protein synthesis. By doing so, and combined with a proper diet, a user may develop lean body mass at a faster rate, more efficiently. Additionally, a user should notice a reduction in recovery time after bouts of intense exercise or weight training.

In one aspect, the Bio-Gro supplement utilizes at least three bio-active components isolated from colostrum. More specifically, the supplement includes **insulin-like growth factor 1 (IGF-1), transforming growth factor-beta 2, and proline-rich peptides (PRP's)**. In various arrangements, the individual concentrations of these bio-active components are engineered to be varied in specific amounts. In other words, the concentrations of the growth factors, such as IGF-1, TGF-β 2, and PRP, are in excess of the concentrations found in normal unprocessed colostrum.

The inclusion of IGF-1 and TGF-β2 enhance the body's protein synthesis. That is, these growth factors promote physiological response to distress signals generated by the body in response to muscle exertion and thereby improve overall protein synthesis. More specifically, **insulin-like growth factor 1 (IGF-1)** is a primary mediator of the effects of growth hormone (GH) made in anterior pituitary gland, which is released into the bloodstream and then stimulates systemic body growth. IGF-1 has been identified as having growth-promoting effects on almost every cell in the body, especially skeletal muscle, cartilage, bone, liver, kidney, nerves, skin, hematopoietic cell, and lungs. **Transforming growth factor-beta 2 (TGF-β2)** are multifunctional peptides that regulate proliferation, differentiation, adhesion, migration, and other functions in many cell types by transducing their signal through cell membranes. PRP's have the ability to modulate the immune system, increasing its activity level in the case of a challenge, such as muscle exertions. When cell damage is detected, chemical signals go out to mobilize other cells to begin repair. PRP's are one of the primary signals that go out at this time. By increasing the PRP's available to the body, the signal level generated by the body may be amplified, thereby helping to improve recovery.

In addition to the above noted bio-active components, the Bio-Gro supplement also includes additional important components, some of which may likewise be isolated and concentrated from colostrum. More specifically, the Bio-Gro supplement further includes **Immunoglobulin A (IgA),** which is an antibody that plays a critical role in mucosal immunity. Stated otherwise, IgA is an anti-inflammatory that assists in the recovery of white blood cells. In addition, **Lactoferrin (LF)** is included in the Bio-Gro supplement. LF, like IgA, stimulates the immune system, and has been reported to help improve connective tissue in humans. An additional component to the Bio-Gro supplement includes **Fibroblast Growth Factors (FGF's),** which are a family of growth factors involved in angiogenesis, wound healing, and embryonic development; and **Epidermal Growth Factor (EGF)** which is a growth factor that stimulates cell growth, proliferation, and differentiation; and/or **Platelet-Derived Growth Factor** (PDGF), which regulate cell growth and division.

Future Research on Bio-Active Peptides

The bio-active peptide supplement should be utilized (e.g., ingested daily) in conjunction with a training regimen to produce one or more enhanced physiological effects. In this regard, the bio-active supplement/product, Bio-Gro, is currently being studied to potentially help increase the following physiological responses:

- **Greater muscle hypertrophy than training alone.**
- **Greater muscle strength and power than training alone.**
- **Greater neuromuscular efficiency changes than training alone (e.g., less muscle to do more work.)**
- **Greater skeletal muscle physiological cross-sectional area than training alone.**
- **Greater muscle quality changes than training alone.**
- **Greater anabolic hormone response than training alone.**
- **Effectiveness of muscle growth *greater* than whey protein ingested only.**

In summary, bio-active peptides represent an exciting new development in the frontier of drug-free performance enhancement. It's apparent; bio-actives derived from milk proteins offer a promising approach for the promotion of health and performance by means of daily supplementation. As such, the potential benefits of bio-active peptides have become a recent point of interest because of their prospective in forging a new development in commercially available supplements that contain these bio-actives. Hence, the exploration of bio-active peptides for improving performance is getting further underway and has thus far seen promising results that will positively change the sports supplementation industry forever. Industry leaders have emerged with products, such as the Bio-Pro Bio-Active Peptides found only in Bio-Gro, that have been shown to improve strength, increase muscle cross-sectional area, decrease inflammation, and improve overall recovery. As science improves on the power of these tiny sub-fractions of proteins, especially highly concentrated specifically engineered varieties, and the research on athletes catches up, anecdotal claims will be met by real science, and athletes and general fitness enthusiasts will have found a faster way to get to their goals.

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