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REPORT

The New Faces Of Whey

Numerous studies on whey proteins demonstrate their potential for improving immunity, boosting glutathione and protecting against cancer. Sales of whey proteins are increasing worldwide and there has been a severe shortage of whey as producers attempt to meet the high consumer demand.

Researchers are finding possible medical uses for whey that are quite unexpected and different from whey's traditional role as an immune booster and anticancer functional food. As with all cutting edge science, the new research is preliminary but exciting nonetheless. For example, whey may be able to reduce stress and depression by lowering cortisol and increasing brain serotonin, improve liver function (in those suffering from certain forms of hepatitis) and reduce blood pressure. We cover these and other findings in this article.



by Will Brink

One major area of research and profit for drug companies over the past decade has been examining the role of brain serotonin level and mood. Some of the most profitable drugs on the market increase serotonin levels. For example, Prozac is a well-known drug whose major effect is believed to be via its effects on serotonin levels in the brain. Prozac, as well as other anti-depressant drugs such as Paxil, Celexa and Zoloft, increase levels of serotonin. These drugs are called selective serotonin reuptake inhibitors, or SSRIs. None of these drugs, however, produce serotonin directly. Supplements such as the amino acid L-tryptophan, 5HTP and others work to increase serotonin by converting directly to serotonin in the brain.

Increased brain serotonin levels enable people to better cope with stress, whereas a decline in serotonin activity is associated with depression and anxiety. Elevated levels of serotonin in the body often result in the relief of depression, as well as a substantial reduction in pain sensitivity, anxiety and stress. It has also been theorized that a diet-induced increase in tryptophan may increase brain serotonin levels.

One recent study examined whether alpha-lactalbumin—a major subfraction found in whey that has an especially high tryptophan content—would increase plasma tryptophan levels as well reduce depression and cortisol concentrations in subjects under acute stress considered to be vulnerable to stress. It's important to note that levels of alpha-lactalbumin and other important subfractions can vary greatly and depend on how the whey is processed. Some whey products on the market contain very little alpha-lactalbumin and other active subfractions (i.e. lactoferrin). The researchers examined 29 "highly stress-vulnerable subjects" and 29 "relatively stress-invulnerable" subjects using a double blind, placebo-controlled study design. The study participants were exposed to experimental stress after eating a diet enriched with either alpha-lactalbumin (found in whey) or sodium-caseinate, another milk based protein. They researchers looked at:

- Diet-induced changes in the plasma tryptophan and its ratio to other large neutral amino acids
- Prolactin levels
- Changes in mood and pulse rate
- Cortisol levels (which were assessed before and after the stressor)

Amazingly, the ratio of plasma tryptophan to the other amino acids tested was 48% higher after the alpha-lactalbumin diet than after the casein diet! This was accompanied by a decrease in cortisol levels and higher prolactin concentration. Perhaps most important and relevant to the average person reading this article, they found "reduced depressive feelings" when test subjects were put under stress. They concluded, "Consumption of a dietary protein enriched in tryptophan increased the plasma Trp-LNAA ratio and, in stress-vulnerable subjects, improved coping ability, probably through alterations in brain serotonin." This effect was not seen in the sodium-caseinate group. If other studies can confirm these findings, whey may turn out to be yet another safe and effective supplement in the battle against depression and stress.

In the years of working with people taking whey, it was not uncommon for them to report that they just felt better, but I had no useful explanation as to why. This study may very well explain the anecdotal reports.

The protein alpha-lactalbumin increases the plasma ratio of tryptophan to the other large neutral amino acids, and in vulnerable subjects raises brain serotonin activity, reduces cortisol concentration, and improves mood under stress.[1]



Whey and HIV

One area readers are probably familiar with is whey's ability to suppress viral loads and improve immunity in people with HIV. HIV infection is characterized by increased oxidative stress and a systemic deficiency of glutathione (GSH). The importance of GSH for the proper function of the immune system cannot be overstated. GSH is arguably the most important water-soluble antioxidant found in the body. The concentration of intracellular GSH is directly related to lymphocytes' reactivity to a challenge, which suggests that intracellular GSH levels are one way to modulate immune function. GSH is a tripeptide made up the amino acids L-cysteine, L-glutamine and glycine. Of the three, cysteine is the main source of the free sulfhydryl group of GSH and is a limiting factor in the synthesis of GSH. Because GSH is known to be essential to immunity, oxidative stress and general well-being, different strategies to supplement cysteine have been used to increase glutathione levels in HIV-infected individuals. For example, NAC (N-acetyl-cysteine) and alpha-lipoic acid are well known for increasing levels of GSH. Whey also appears to be a potent GSH-raising nutrient.

A recent study evaluated the effects of supplementation with two different whey protein formulas on GSH levels and oxidative stress and immune status in HIV-infected patients.[2] Using a prospective double blind design, 30 patients-25 men and 5 women-with HIV infection were randomized to receive 45 grams per day of one of two whey formulas for two weeks. The researchers looked at various indices of oxidative stress, such as:

- Plasma concentrations of total, reduced and oxidized GSH
- Plasma levels of TNF-alpha, Interleukins 2 and 12

Following two weeks of oral supplementation with whey proteins, plasma GSH levels increased in one group by 44%, while the difference in the second group did not reach significance. Interestingly, plasma concentrations of TNF-alpha and interleukins 2 and 12 remained unchanged in both groups. However, the short duration of the study might have found different results in TNF and the interleukins had the study run longer. The researchers concluded, "In glutathione-deficient patients with advanced HIV-infection, short-term oral supplementation with whey proteins increases plasma glutathione levels." The real question remains, Would this use of whey and increase in GSH translate into a more favorable course of the disease? The answer is it should, could, and probably would, but a long-term follow up study is needed for definitive answers. This study adds to the other growing research on the power of whey to possibly modulate HIV infection in a favorable direction.

Perhaps the most interesting finding of this study is the fact it confirms yet again that not all whey products are created equal, as only one of the groups had an increase in GSH. It's yet more conformation that not all whey products on the market will have this effect on GSH, and that the quality of the product matters.

Another major concern for people with HIV is the loss of body weight, known as wasting syndrome. This steady loss of weight will be accompanied by significant loss of muscle mass or body cell mass (BCM), which is needed to support life itself. In fact,

A major concern for people with HIV is the loss of weight, known as wasting syndrome. As the name implies, wasting syndrome involves a loss of body weight. One recent studied concluded a combination treatment with whey and weight training "provided a patient-directed, non-pharmaceutical, low-cost approach to augment body cell mass in catabolic HIV-infected patients."

this steady loss of lean body mass (LBM) or BCM is strongly correlated with time of death showing just how important it is for people with HIV to maintain their LBM. Some researchers have opted to use drugs such as human growth hormone (HGH), anabolic steroids and other drugs in an attempt to prevent muscle wasting or reverse wasting in patients. These pharmaceutical strategies, although often effective and worthwhile, come with their own set of potential problems and high financial costs. One recent studied called "Effects of whey protein and resistance exerciseon body composition and muscle strength in women with HIV infection" examined the combination of whey protein



Increased brain serotonin levels

and progressive resistance exercise (weight lifting) upon body composition and physical function in 30 malnourished HIV-infected women. The women were studied for a six-week control period, and then randomized to whey alone, weight training or a combination of both for 14 weeks. As expected, the combination group (weight training plus whey) had the greatest effects and increases in strength without large increases in body fat. The researchers concluded that the combination treatment with whey and weight training "...provided a patient-directed, nonpharmaceutical, low-cost approach to augment BCM in catabolic HIV-infected patients." People with HIV should employ weight training and whey as a low cost, safe treatment for preserving essential LBM.

enable people to better cope with stress, whereas a decline in serotonin activity is associated with depression and anxiety.

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Possible effects on blood pressure

As we age there is a loss of arterial elasticity, which is a cause of high blood pressure. Another major cause of hypertension is an enzyme secreted by the kidneys called angiotension-converting enzyme (ACE). Angiotension-converting enzyme (ACE) has been classically associated with the renin-angiotension system, which regulates peripheral blood pressure. People with high blood pressure are often prescribed drugs such as Zestril, Capoten and Vasotec, referred to as "angiotension-converting enzyme inhibitors" or ACE inhibitors for short. By blocking the effects of ACE, blood pressure can be brought under control in the majority of people with hypertension.

Whey peptides, known as Lactokinins, were recently shown to be mild ACE inhibitors in vitro.[3] While they do not have the inhibitory potency of the drugs mentioned above used in the treatment of hypertension, the researchers concluded, "...these naturally occurring peptides may represent nutraceutical/functional food ingredients for the prevention/treatment of high blood pressure." Clearly more research is needed, but if confirmed by future research, this could be yet another use for whey proteins.

Effects on hepatitis

Considering the importance of glutathione (GSH) for liver function and the resulting oxidative stress that accompanies hepatitis, researchers looked to see what affect high quality whey would have on laboratory indices of viral hepatitis and liver function. In an open clinical study researchers looked at the efficacy of whey protein vs. casein fed to 25 patients suffering from either hepatitis B or C. Twelve grams of either whey or casein as food was given twice a day, in the morning and evening, for 12 weeks. The researchers looked at

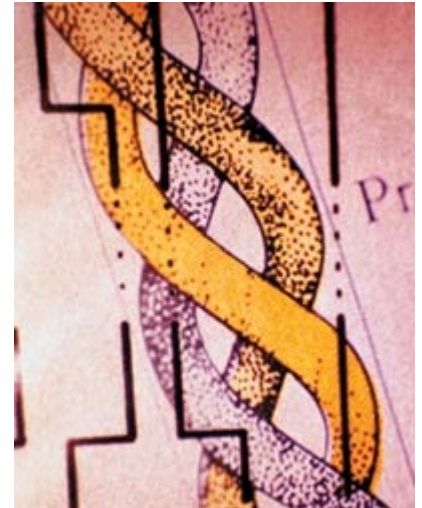
- Serum alanine aminotransferase (ALT)-an indicator of liver stress and function
- Serum glutathione (GSH)
- Serum lipid peroxide levels-an indicator of oxidative stress
- Interleukin (IL)-2 levels-a pro inflammatory interleukin
- Natural killer (NK) cell activity

Amazingly, after the 12-week period, the hepatitis B group getting the whey showed a "significant" decrease in serum lipid peroxides, with an increase in plasma glutathione levels in five of the eight subjects. A decrease was shown in Interleukin (IL)-2 levels with a significant increase in natural killer (NK) cell activity. Most important, there was a drop in serum alanine aminotransferase (ALT) activity, indicating reduction in liver damage caused by the hepatitis B virus. Unfortunately, there were no significant changes in the 17 patients with hepatitis C. Based on this one study, it would appear that whey might be a safe therapy for improving liver function in patients with chronic hepatitis B but not hepatitis C.[4] Since the mechanisms of whey's actions would appear to benefit hepatitis C patients, we eagerly look forward to the results of additional clinical studies.

Whey protects the stomach as well as antiulcer drugs

An ever-growing body of studies has shown that whey proteins and their subfractions have a wide range of biological activities. One area that has not been fully explored is the potential role of whey protein in the protection of the gastrointestinal system. One recent study investigated the effect of either whey or casein protein on gastric mucosal injury by using two ulcer models in rats.[5] Gastric mucosal injury was induced by either alcohol (ethanol) or water-immersion restraint stress where the poor rats are put in water at 23 degrees C for 7 hours.

Whey or casein was given to the rats 30 min before the induction of gastric injury. Whey is a complex protein made up of many smaller protein subfractions (peptides). Each of the subfractions found in whey has its own unique biological properties. Interestingly, one of the major subfractions in whey (alpha-lactalbumin) was shown to have a "...marked protective effect against ethanol-induced gastric injury, with the same potency as that of the typical antiulcer agent, Selbex," according to the researchers. As expected, whey protein isolate (WPI) also protected against gastric injury, as it contains high amounts of alpha-lactalbumin,



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while casein showed no effect.

Alpha-lactalbumin showed dose-dependent protection against gastric injury caused by alcohol or stress. The effect appears to be in part due to prostaglandin synthesis caused by the alpha-lactalbumin found in the whey, but effects on GSH in tissues probably played a key role. The researchers concluded, "These results indicate that alpha-LA (a component found in whey) has marked antiulcer activity as an active component of cow's milk protein, and suggest that alpha-LA intake may serve to protect against gastric mucosal injury, in part through endogenous prostaglandin synthesis." Again, human studies are needed to come to definitive conclusions about the role a high quality whey protein may play in the development and protection against ulcers and other pathologies/injuries to the stomach, but it's a potentially important finding to the millions of people with various gastrointestinal problems.

Chronic fatigue

Chronic fatigue syndrome (CFS) has been a vexing problem for both clinicians and patients alike. Finding clear associations between people who suffer from CFS has been difficult. There have been, however, some similarities among groups of people with CFS. In a large proportion of people with CFS, abnormalities are often found in both humoral and cellular immunity. The exact cause of this is not fully understood. One fairly consistent finding in people with CFS is an impaired lymphocyte (T-cell) responses to a challenge. That is, the lymphocyte does not respond appropriately or rapidly when presented with an immune challenge. As early research has shown, the ability of lymphocytes to react to an immune challenge is directly related to their GSH status.[6] Also, continued use of GSH by lymphocytes may lead to cellular GSH depletion and immune failure. One hypothesis put forth by Dr. Bounous from the Department of Surgery at McGill University, is the idea that the competition for GSH precursors over time may lead to muscle fatigue (myalgia) and other symptoms associated with CFS. He states: "Because GSH is also essential to aerobic muscular contraction, an undesirable competition for GSH precursors between the immune and muscular systems may develop. It is conceivable that the priority of the immune system for the survival of the host has drawn to this vital area the ever-diminishing GSH precursors, thus depriving the skeletal muscle of adequate GSH precursors to sustain a normal aerobic metabolism resulting in fatigue and eventually myalgia."



Because whey is the most effective way to deliver precursors for GSH synthesis, as well as being shown to raise GSH levels in humans and animals, it is theorized that whey may be especially effective for people suffering from CFS. Although large-scale studies with CFS and whey have yet to be done, the idea makes perfect sense and it may be worth a try for people with CFS to use whey on a regular basis.

Whey and performance

Finally, most athletes know of whey as a high quality protein with a very high biological value (BV) rating. It's no surprise that athletes and active people have made whey based protein supplements the best selling on the market. However, whey may in fact have direct effects on performance. Many studies have found that oxidative stress contributes to muscular fatigue and some studies have found the use of antioxidants may improve performance. As mentioned previously, GSH is the major intracellular water-soluble antioxidant in the body, which is involved in the recycling of other antioxidants.

Twenty healthy young adults (10 men, 10 women) were supplemented with either whey or casein for three months. The researchers looked at:

- Muscular performance-as assessed by whole leg isokinetic cycle testing
- Lymphocyte GSH levels-as a marker of tissue GSH

As one would expect, they found no baseline differences in peak power or work capacity between the whey and casein groups. However, after treatment, a follow-up on 18 subjects-nine who received the whey and nine who received the casein (considered a placebo in this study)-were analyzed. Both peak power and work capacity increased significantly in the whey group, with no changes found in the casein group.[7] Lymphocyte GSH also increased by over 35% in the group receiving the whey with no change in the group getting casein. The researchers concluded, "This is the first study to demonstrate that prolonged supplementation with a product designed to augment antioxidant defenses resulted in improved volitional performance." This along with previous studies make it clear that whey is the protein supplement of choice for athletes for a wide variety of reasons, one of which may be improved performance during endurance exercise.

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