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(54) Titre : COMPOSITION NUTRITIONNELLE ET METHODE POUR ACCROITRE L'ABSORPTION ET LA RETENTION DE CREATINE DANS LES MUSCLES SQUELETTIQUES, ACCROITRE LA MASSE ET LA FORCE MUSCULAIRES, ACCROITRE LA CAPACITE D'EXERCICE ET CONTRIBUER AU RETABLISSEMENT APRES EXERCICE

(54) Title: NUTRITIONAL COMPOSITION AND METHOD FOR INCREASING CREATINE UPTAKE AND RETENTION IN SKELETAL MUSCLE, INCREASING MUSCLE MASS AND STRENGTH, INCREASING EXERCISE CAPACITY AND FOR AIDING RECOVERY FOLLOWING EXERCISE

(57) **Abrégé/Abstract:**

The present invention relates to a dietary supplement that comprises at least Creatine or derivatives thereof, Taurine or derivatives thereof and a source of Phosphate. The dietary supplement may further comprise one or more of the following: Double Fermented Triticum aestivum, Dextrose, Isomalt, Trehalose, D-Mannose, Mulberry extract, Enicostemma littorale Blume, Scoparia dulcis, Tarragon extract, Andrographis paniculata, Chromium or derivatives thereof, Glutamine and Alpha Lipoic Acid. The present invention may also provide a method for increasing Creatine uptake and retention in skeletal muscle, increasing muscle mass and strength, increasing exercise capacity and aiding in recovery following exercise as well as supporting the immune system during periods of intense training.

### Abstract

The present invention relates to a dietary supplement that comprises at least Creatine or derivatives thereof, Taurine or derivatives thereof and a source of Phosphate. The dietary supplement may further comprise one or more of the following: Double Fermented *Triticum aestivum*, Dextrose, Isomalt, Trehalose, D-Mannose, Mulberry extract, *Enicostemma littorale* Blume, *Scoparia dulcis*, Tarragon extract, *Andrographis paniculata*, Chromium or derivatives thereof, Glutamine and Alpha Lipoic Acid. The present invention may also provide a method for increasing Creatine uptake and retention in skeletal muscle, increasing muscle mass and strength, increasing exercise capacity and aiding in recovery following exercise as well as supporting the immune system during periods of intense training.

**Nutritional Composition and Method for Increasing Creatine Uptake and Retention in Skeletal Muscle, Increasing Muscle Mass and Strength, Increasing Exercise Capacity and for Aiding Recovery Following Exercise**

5 **Field of the Invention**

The present invention relates to the composition of a dietary supplement provided for increasing Creatine uptake and retention in skeletal muscle, increasing muscle mass and strength, increasing exercise capacity and aiding in recovery following exercise as well as providing support for the immune system during intense periods of exercise. Furthermore, a method for achieving the same by way of administration of the composition is presented.

**Summary of the Invention**

The foregoing needs, and other needs and objectives which will become apparent in the following description, are achieved in the present invention which comprises a dietary composition and method for enhancing Creatine uptake and retention in skeletal muscle, increasing muscle mass and strength, increasing lean muscle mass, and supporting the immune system of an individual, e.g., a human or an animal, during intense training periods. According to an embodiment of the present invention, there are provided compositions and methods which minimize catabolism and promote muscle anabolism, particularly in response to exercise. For example the compositions and methods may allow an individual to increase muscle size, strength or endurance training as well as reduce recovery time and facilitate an increased training volume leading to the same.

According to an embodiment of the present invention, there are provided compositions and methods which comprise at least a combination of Creatine or derivatives thereof, Taurine or derivatives thereof and a source of Phosphate.

5 According to additional or alternative embodiments of the present invention, there are provided compositions and methods that further comprise at least one of Double Fermented Triticum aestivum, Dextrose, Isomalt, Trehalose, D-Mannose, an extract of Mulberry, *Enicostemma littorale* Blume, *Scoparia dulcis*, an extract of Tarragon, *Andrographis paniculata*, Chromium or derivatives thereof, Glutamine and Alpha Lipoic Acid.

## 10 **Detailed Description of the Invention**

In the following description, for the purposes of explanation, numerous specific details are set forth in order to provide a thorough understanding of the present invention. It will be apparent, however, to one skilled in the art that the present invention may be practiced without one or more of these specific details.

15 The present invention, according to various embodiments thereof, is directed to a dietary supplement for increasing Creatine uptake and retention in skeletal muscle, increasing muscle mass and strength, increasing exercise capacity and aiding in post-exercise recovery as well as providing support for the immune system during intense exercise training periods. The present invention  
20 comprises at least a source of Creatine or derivative thereof, Taurine or derivative thereof and a source of Phosphate. According to various embodiments, the present invention may further comprise combinations of Double Fermented Triticum aestivum, Dextrose, Isomalt, Trehalose, D-Mannose,

an extract of Mulberry, *Enicostemma littorale* Blume, *Scoparia dulcis*, an extract of Tarragon, *Andrographis paniculata*, Chromium or derivatives thereof, Glutamine and Alpha Lipoic Acid.

### Definitions

5 As used herein, "Carbohydrate" refers to at least a source of carbohydrates such as, but not limited to, monosaccharides, disaccharides, oligosaccharides, polysaccharides or derivatives thereof.

As used herein, "Creatine" refers to the chemical N-methyl-N-guanyl Glycine, (CAS Registry No. 57-00-1), also known as, (alpha-methyl guanido) acetic acid, N-(aminoiminomethyl)-N-glycine, Methylglycocyanine, 10 Methylguanidoacetic Acid, or N-Methyl-N-guanylglycine. Additionally, as used herein, "Creatine" also includes derivatives of Creatine such as esters, and amides, and salts, as well as other derivatives, including derivatives that become active upon metabolism. Furthermore, Creatinol (CAS Registry No. 6903-79-3), 15 also known as Creatine-O-Phosphate, N-methyl-N-(beta-hydroxyethyl)guanidine O-Phosphate, Aplodan, or 2-(carbamimidoyl-methyl-amino)ethoxyphosphonic acid, is henceforth in this disclosure considered to be a Creatine derivative.

As used herein, "Phosphate" refers to at least a source of Phosphate ions such as, but not limited to, Dipotassium Phosphate, Disodium Phosphate, 20 Magnesium Phosphate or derivatives thereof.

Carbohydrate ingestion is known to stimulate the secretion of insulin which in turn facilitates the uptake of glucose into skeletal muscle via glucose transporter 4 (GLUT4) translocation (Wang W, Hansen PA, Marshall BA,

Holloszy JO, Mueckler M. Insulin unmasks a COOH-terminal Glut4 epitope and increases glucose transport across T-tubules in skeletal muscle. *J Cell Biol.* 1996 Oct;135(2):415-30). Glucose is then converted to and stored as glycogen and triglycerides. Concomitant with this, insulin inhibits the release and synthesis of glucose (Khan AH, Pessin JE. Insulin regulation of glucose uptake: a complex interplay of intracellular signalling pathways. *Diabetologia.* 2002 Nov;45(11):1475-83). Moreover, insulin also plays an important role in protein metabolism where it inhibits the breakdown of protein or proteolysis (Volpi E and Wolfe B. Insulin and Protein Metabolism. In: *Handbook of Physiology*, L. Jefferson and A. Cherrington editors. New York: Oxford, 2001, p. 735-757; Boirie Y, Gachon P, Cordat N, Ritz P, Beaufrere B. Differential insulin sensitivities of glucose, amino acid, and albumin metabolism in elderly men and women. *J Clin Endocrinol Metab.* 2001 Feb;86(2):638-44). Furthermore, insulin promotes the uptake of amino acids into muscle and stimulates protein synthesis (Biolo G, Declan Fleming RY, Wolfe RR. Physiologic hyperinsulinemia stimulates protein synthesis and enhances transport of selected amino acids in human skeletal muscle. *J Clin Invest.* 1995 Feb;95(2):811-9), particularly following exercise (Biolo G, Williams BD, Fleming RY, Wolfe RR. Insulin action on muscle protein kinetics and amino acid transport during recovery after resistance exercise. *Diabetes.* 1999 May;48(5):949-57). Insulin has also been shown to stimulate Creatine uptake by muscle cells (Odoom JE, Kemp GJ, Radda GK. regulation of total creatine content in a myoblast cell line. *Mol Cell Biochem.* 1996 May 24;158(2):179-88). Alpha Lipoic Acid has been shown to have insulin-like

properties, which further aid in the retention of Creatine. (Streeper RS, Henriksen EJ, Jacob S, Hokama JY, Fogt DL, Tritschler HJ. Differential effects of lipoic acid stereoisomers on glucose metabolism in insulin-resistant skeletal muscle. *Am J Physiol.* 1997 Jul;273(1 Pt 1):E185-91; Ziegler D, Hanefeld M, Ruhnau KJ, Hasche H, Lobisch M, Schutte K, Kerum G, Malessa R. Treatment of symptomatic diabetic polyneuropathy with the antioxidant alpha-lipoic acid: a 7-month multicenter randomized controlled trial (ALADIN III Study). *ALADIN III Study Group. Alpha-Lipoic Acid in Diabetic Neuropathy. Diabetes Care.* 1999 Aug;22(8):1296-301). Via the combination of Creatine with Alpha Lipoic Acid and a small amount of carbohydrate, Creatine retention as compared to Creatine and carbohydrate alone is significantly improved (Burke DG, Chilibeck PD, Parise G, Tarnopolsky MA, Candow DG. Effect of alpha-lipoic acid combined with creatine monohydrate on human skeletal muscle creatine and phosphagen concentration. *Int J Sport Nutr Exerc Metab.* 2003 Sep;13(3):294-302). Therefore, it is deemed to be advantageous that, for the purposes of Creatine retention, the actions of insulin be enhanced. Furthermore, it may be advantageous to increase the activity and availability of Creatine in skeletal muscle.

Combinations comprising some of the aforementioned ingredients have been shown to offer further benefit to muscle building and increasing strength. In one clinical trial, 32 males were divided into four groups of eight subjects. Group 1 received a combination of Creatine / Dextrose / Taurine / Alpha Lipoic Acid, Group 2 received Creatine plus grape juice, Group 3 received Creatine plus water, and group 4 a placebo. At Day 28 of the experiment, Group 1 had

demonstrated greater improvements in body composition and muscular endurance as compared to the other three groups (Kalman DS, Colker CM, Swain MA, Shi Q, Maharam LG. A double-blind, randomized clinical trial evaluating different creatine monohydrate formulations in resistance trained  
5 males. Med Sci Sports Exerc. 2000, 32(5), Supplement abstract 562). In a further study, Creatine / Dextrose / Alpha Lipoic Acid was found to provide improved results versus supplementation with whey protein alone in terms of muscle mass gain (Kalman DS, Colker CM, Swain MA, Antonio J. A Double-Blind Clinical  
10 Evaluation Comparing Two Popular Dietary Supplements Purported to Enhance Lean Body Mass. FASEB. 2000,14(4):A619). In an eight week study which included diet and weight training, subjects consuming a combination comprising Creatine / Dextrose / Taurine / Ascorbic Acid / Chromium / Alpha Lipoic Acid / Phosphorus gained significantly more mass than subjects consuming Protein /  
15 S, Phillips SM. Creatine-dextrose and protein-dextrose induce similar strength gains during training. Med Sci Sports Exerc. 2001 Dec;33(12):2044-52).

Not wishing to be bound by theory, it is herein believed that the activity of insulin initiated by the ingestion of carbohydrates, such as Dextrose as  
20 comprised in the present invention, can be enhanced and sustained by insulin potentiators such as, including but not limited to, Taurine, Alpha Lipoic Acid, an extract of Mulberry, Chromium, Glutamine, *Encostemma littorale Blume*, *Scoparia dulcis*, an extract of Tarragon and *Andrographis paniculata*. In another embodiment, the present invention may comprise one or more of Isomalt,



Trehalose or D-Mannose to further potentiate the secretion or activity of insulin. The enhanced activity of insulin may facilitate increased uptake and retention of Creatine, as incorporated into the present invention, by skeletal muscle. Subsequently, the increase in Creatine retention may facilitate increased muscle growth, increased muscle endurance and reduced post-exercise recovery time by virtue of the biological role of Creatine. Furthermore, advantageously, the biological role of Creatine may be aided by ensuring adequate Phosphate availability by the addition of supplemental Phosphates.

### **Creatine**

10 Creatine is a naturally occurring amino acid derived from the amino acids glycine, arginine, and methionine. Although it is found in meat and fish, it is also synthesized by humans. Creatine is predominantly used as a fuel source in muscle. About 65% of Creatine is stored in muscle as Phosphocreatine (Creatine bound to a Phosphate molecule) (Casey A, Constantin-Teodosiu D, 15 Howell S, Hultman E, Greenhaff PL. Metabolic response of type I and II muscle fibers during repeated bouts of maximal exercise in humans. *Am J Physiol.* 1996 Jul;271(1 Pt 1):E38-43). Muscular contractions are fueled by the dephosphorylation of adenosine triphosphate (ATP) to produce adenosine diphosphate (ADP) and without a mechanism to replenish ATP stores, the supply 20 of ATP would be totally consumed in 1-2 seconds (Casey A, Greenhaff PL. Does dietary creatine supplementation play a role in skeletal muscle metabolism and performance? *Am J Clin Nutr.* 2000 Aug;72(2 Suppl):607S-17S). Phosphocreatine serves as a major source of Phosphate from which ADP is

regenerated to ATP. Six seconds following the commencement of exercise, muscular concentrations of Phosphocreatine drop by almost 50% (Gaitanos GC, Williams C, Boobis LH, Brooks S. Human muscle metabolism during intermittent maximal exercise. *J Appl Physiol.* 1993 Aug;75(2):712-9).

5 Creatine supplementation has been shown to increase the concentration of Creatine in the muscle (Harris RC, Soderlund K, Hultman E. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. *Clin Sci (Lond).* 1992 Sep;83(3):367-74) and further said supplementation enables an increase in the resynthesis of Phosphocreatine  
10 (Greenhaff PL, Bodin K, Soderlund K, Hultman E. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. *Am J Physiol.* 1994 May;266(5 Pt 1):E725-30) leading to a rapid replenishment of ATP within the first two minutes following the commencement of exercise.

In the early 1990's it was first clinically demonstrated that supplemental  
15 Creatine can improve strength and reduce fatigue (Greenhaff PL, Casey A, Short AH, Harris R, Soderlund K, Hultman E. Influence of oral creatine supplementation of muscle torque during repeated bouts of maximal voluntary exercise in man. *Clin Sci (Lond).* 1993 May;84(5):565-71). Resistance training with supplemented creatine experiments display a result of increased strength  
20 and fat-free mass over a placebo in sedentary females (Vandenberghe K, Goris M, Van Hecke P, Van Leemputte M, Vangerven L, Hespel P. Long-term creatine intake is beneficial to muscle performance during resistance training. *J Appl Physiol.* 1997 Dec;83(6):2055-63) and in male football players (Vandenberghe K,

Goris M, Van Hecke P, Van Leemputte M, Vangerven L, Hespel P. Long-term creatine intake is beneficial to muscle performance during resistance training. *J Appl Physiol.* 1997 Dec;83(6):2055-63). In addition to increasing fat-free mass and strength, Creatine supplementation increases muscle fiber cross sectional  
5 area (Volek JS, Duncan ND, Mazzetti SA, Staron RS, Putukian M, Gomez AL, Pearson DR, Fink WJ, Kraemer WJ. Performance and muscle fiber adaptations to creatine supplementation and heavy resistance training. *Med Sci Sports Exerc.* 1999 Aug;31(8):1147-56) thereby increasing muscle volume. High-intensity exercise performance of both males and females is also improved by  
10 supplemental Creatine (Tarnopolsky MA, MacLennan DP. Creatine monohydrate supplementation enhances high-intensity exercise performance in males and females. *Int J Sport Nutr Exerc Metab.* 2000 Dec;10(4):452-63; Burke DG, Silver S, Holt LE, Smith Palmer T, Culligan CJ, Chilibeck PD. The effect of continuous low dose creatine supplementation on force, power, and total work. *Int J Sport  
15 Nutr Exerc Metab.* 2000 Sep;10(3):235-44). Creatine supplementation may also benefit individuals with muscle dystrophy disorders by reducing muscle loss (Walter MC, Lochmuller H, Reilich P, Klopstock T, Huber R, Hartard M, Hennig M, Pongratz D, Muller-Felber W. Creatine monohydrate in muscular dystrophies: A double-blind, placebo-controlled clinical study. *Neurology.* 2000 May  
20 9;54(9):1848-50).

Furthermore, there is evidence that Creatine may have antioxidant properties (Lawler JM, Barnes WS, Wu G, Song W, Demaree S. Direct antioxidant properties of creatine. *Biochem Biophys Res Commun.* 2002 Jan

11;290(1):47-52; Sestili P, Martinelli C, Bravi G, Piccoli G, Curci R, Battistelli M, Falcieri E, Agostini D, Gioacchini AM, Stocchi V. Creatine supplementation affords cytoprotection in oxidatively injured cultured mammalian cells via direct antioxidant activity. *Free Radic Biol Med.* 2006 Mar 1;40(5):837-49). The  
5 antioxidant activity of Creatine may additionally aid post-exercise muscle recovery.

Creatine retention has been shown to be markedly improved by the concomitant ingestion with carbohydrates, up to 60% better, which may further be related to increased insulin concentration (Green AL, Hultman E, Macdonald  
10 IA, Sewell DA, Greenhaff PL. Carbohydrate ingestion augments skeletal muscle creatine accumulation during creatine supplementation in humans. *Am J Physiol.* 1996 Nov;271(5 Pt 1):E821-6). Furthermore, glucose and Creatine uptake by muscle cells has been shown to be stimulated by insulin (Odoom JE, Kemp GJ, Radda GK. regulation of total creatine content in a myoblast cell line. *Mol Cell  
15 Biochem.* 1996 May 24;158(2):179-88). Thus, the ingestion of Creatine combined with a source of carbohydrates is recommended to improve retention. It may also be beneficial to include a source of protein at the time of Creatine ingestion (Steenge GR, Simpson EJ, Greenhaff PL. Protein- and carbohydrate-induced augmentation of whole body creatine retention in humans. *J Appl  
20 Physiol.* 2000 Sep;89(3):1165-71).

U.S. Patent No. 5,767,159 purports to describe a method for increasing muscle capacity and replenishing ATP by administering daily Creatine in healthy mammals. The amount of said Creatine is at least 0.2-0.4 g per kg body weight

and not less than 15 g in a 70 kg mammal to be taken for at least 2 days but not more than 7 days. The Creatine is administered in solution which may further include other conventional nutrients such as lipids, carbohydrates, amino acids, electrolytes, trace elements and vitamins.

5 U.S. Patent No. 5,968,544 purports to describe compositions containing Creatine for human consumption suitable for use in a drink or as dry powder stable for storage. The Creatine is provided in an acidic yogurt-based semi-liquid composition or forms an acidic solution when mixed with water.

10 U.S. Patent No. 5,973,199 purports to describe compositions for water soluble Creatine salts usable in foods.

U.S. Patent No. 5,968,900 purports to describe compositions and methods for increasing Creatine and glycogen concentration in muscle by increasing blood plasma insulin concentration. In one described embodiment, the compositions described are composed of Creatine or Creatine derivatives with a carbohydrate, 15 wherein the carbohydrate is said to cause an increase in blood plasma insulin levels, which results in increases Creatine retention.

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement includes Creatine or derivatives thereof. A serving of the dietary supplement may include from about 20 3 g to about 15 g of Creatine or derivatives thereof. The preferred dosage of a serving of the dietary supplement comprises about 10 g of Creatine or derivatives thereof.

## Taurine

Taurine, an amino acid found primarily in nerve and muscle tissue, is generally considered to be a conditionally-essential amino acid, being only required under certain circumstances. As it is not utilized for protein synthesis,

5 Taurine is found in the free form or in some small peptides. The accumulation of Taurine within cells is mediated via a high affinity sodium-dependent transporter (Ramamoorthy S, Leibach FH, Mahesh VB, Han H, Yang-Feng T, Blakely RD, Ganapathy V. Functional characterization and chromosomal localization of a cloned taurine transporter from human placenta. *Biochem J.* 1994 Jun 15;300 (

10 Pt 3):893-900). The expression of this Taurine transporter is induced by differentiation program of myocytes (muscle cells) (Uozumi Y, Ito T, Hoshino Y, Mohri T, Maeda M, Takahashi K, Fujio Y, Azuma J. Myogenic differentiation induces taurine transporter in association with taurine-mediated cytoprotection in skeletal muscles. *Biochem J.* 2006 Mar 15;394(Pt 3):699-706). Exercise-induced

15 hormones are also known to activate the Taurine transporter (Park SH, Lee H, Park T. Cortisol and IGF-1 synergistically up-regulate taurine transport by the rat skeletal muscle cell line, L6. *Biofactors.* 2004;21(1-4):403-6). Moreover, genetically modified mice lacking the Taurine transporter have depleted Taurine levels in all muscle and have impaired skeletal muscle function (Warskulat U,

20 Flogel U, Jacoby C, Hartwig HG, Thewissen M, Merx MW, Molojavyi A, Heller-Stilb B, Schrader J, Haussinger D. Taurine transporter knockout depletes muscle taurine levels and results in severe skeletal muscle impairment but leaves cardiac function uncompromised. *FASEB J.* 2004 Mar;18(3):577-9)

One of the main roles of Taurine is the regulation of fluid balance and is released by contracting muscles (Cuisinier C, Michotte De Welle J, Verbeeck RK, Poortmans JR, Ward R, Sturbois X, Francaux M. Role of taurine in osmoregulation during endurance exercise. *Eur J Appl Physiol.* 2002 Oct;87(6):489-95). Taurine has also been shown to modulate the contractile function of mammalian skeletal muscle (Bakker AJ, Berg HM. Effect of taurine on sarcoplasmic reticulum function and force in skinned fast-twitch skeletal muscle fibres of the rat. *J Physiol.* 2002 Jan 1;538(Pt 1):185-94). In rats, the Taurine concentration in muscle decreases as a result of exercise (Matsuzaki Y, Miyazaki T, Miyakawa S, Bouscarel B, Ikegami T, Tanaka N. Decreased taurine concentration in skeletal muscles after exercise for various durations. *Med Sci Sports Exerc.* 2002 May;34(5):793-7) and oral supplementation with Taurine has been shown to maintain the concentration of Taurine in muscle and prolong exercise performance (Miyazaki T, Matsuzaki Y, Ikegami T, Miyakawa S, Doy M, Tanaka N, Bouscarel B. Optimal and effective oral dose of taurine to prolong exercise performance in rat. *Amino Acids.* 2004 Dec;27(3-4):291-8; Yatabe Y, Miyakawa S, Miyazaki T, Matsuzaki Y, Ochiai N. Effects of taurine administration in rat skeletal muscles on exercise. *J Orthop Sci.* 2003;8(3):415-9).

In a model of spontaneous diabetes, Taurine supplementation has been shown to improve insulin sensitivity in rats (Nakaya Y, Minami A, Harada N, Sakamoto S, Niwa Y, Ohnaka M. Taurine improves insulin sensitivity in the Otsuka Long-Evans Tokushima Fatty rat, a model of spontaneous type 2 diabetes. *Am J Clin Nutr.* 2000 Jan;71(1):54-8). Furthermore, Taurine improves

glucose metabolism in insulin resistant rats (Nandhini AT, Anuradha CV. Taurine modulates kallikrein activity and glucose metabolism in insulin resistant rats. Amino Acids. 2002;22(1):27-38), suggesting that Taurine has insulin-like properties which may improve Creatine uptake and retention within muscle cells.

5   Supplementation with Taurine has additionally been shown to reduce exercise-induced oxidative damage and enhance recovery (Zhang M, Izumi I, Kagamimori S, Sokejima S, Yamagami T, Liu Z, Qi B. Role of taurine supplementation to prevent exercise-induced oxidative stress in healthy young men. Amino Acids. 2004 Mar;26(2):203-7).

10         In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement includes Taurine or derivatives thereof. A serving of the dietary supplement may include from about 0.5 g to about 3 g of Taurine or derivatives thereof. The preferred dosage of a serving of the dietary supplement comprises about 2.1 g of Taurine or derivatives  
15   thereof.

### **Phosphate**

Phosphate, or phosphorus, is the second most abundant mineral in the body with calcium being the most abundant. As a Phosphate salt with calcium, Phosphate is involved in the formation of bone and teeth. In other salt  
20   complexes, Phosphate is involved in acid-base balance. Phosphate is also important for the structures of DNA and cell membranes. One of the most important roles of Phosphate is energy production in muscle as ATP and Phosphocreatine. Phosphate is also part of a compound in red blood cells known



as 2,3 DPG (2,3-diphosphoglycerate), which facilitates the release of oxygen to the muscle tissues.

Supplemental Phosphate salts have been shown to increase the concentration of 2,3 DPG in red blood cells, increasing VO<sub>2</sub> max (a measure of aerobic fitness) and a reduction in the production of lactate (Cade R, Conte M, Zauner C, Mars D, Peterson J, Lunne D, Hommen N, Packer D. Effects of phosphate loading on 2,3-diphosphoglycerate and maximal oxygen uptake. *Med Sci Sports Exerc.* 1984 Jun;16(3):263-8). Moreover, Phosphate has also been shown to enhance oxygen uptake and run performance without affecting the level of 2,3 DPG (Kreider RB, Miller GW, Williams MH, Somma CT, Nasser TA. Effects of phosphate loading on oxygen uptake, ventilatory anaerobic threshold, and run performance. *Med Sci Sports Exerc.* 1990 Apr;22(2):250-6).

The metabolic rate can also be increased by Phosphate supplementation (Nazar K, Kaciuba-Uscilko H, Szczepanik J, Zemba AW, Kruk B, Chwalbinska-Moneta J, Titow-Stupnicka E, Bicz B, Krotkiewski M. Phosphate supplementation prevents a decrease of triiodothyronine and increases resting metabolic rate during low energy diet. *J Physiol Pharmacol.* 1996 Jun;47(2):373-83).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement includes a source of Phosphate or derivatives thereof. A serving of the dietary supplement may include from about 0.1 g to about 1.5 g of Phosphate or derivatives thereof. The preferred dosage of a serving of the dietary supplement comprises about 0.18 g of elemental Phosphate or derivatives thereof.

## Alpha Lipoic acid

Alpha Lipoic Acid (ALA) is an enzyme found in the cellular energy-producing structures, the mitochondria. ALA works in synergy with vitamins C and E as an antioxidant in both the water- and fat- soluble environments.

5 In rats supplemented with ALA, the negative age-related changes in mitochondrial function, accumulated oxidative damage and metabolic rate were all improved (Hagen TM, Ingersoll RT, Lykkesfeldt J, Liu J, Wehr CM, Vinarsky V, Bartholomew JC, Ames AB. (R)-alpha-lipoic acid-supplemented old rats have improved mitochondrial function, decreased oxidative damage, and increased  
10 metabolic rate. FASEB J. 1999 Feb;13(2):411-8). As such, the antioxidant activity of ALA is likely involved in the prevention of cell death due to an improvement in oxidative stress (Arivazhagan P, Juliet P, Panneerselvam C. Effect of dl-alpha-lipoic acid on the status of lipid peroxidation and antioxidants in aged rats. Pharmacol Res. 2000 Mar;41(3):299-303). Furthermore, ALA has been linked to  
15 a beneficial increase in high-density lipoproteins (Wollin SD, Wang Y, Kubow S, Jones PJ. Effects of a medium chain triglyceride oil mixture and alpha-lipoic acid diet on body composition, antioxidant status, and plasma lipid levels in the Golden Syrian hamster. J Nutr Biochem. 2004 Jul;15(7):402-10) possibly due to its known effects as an antioxidant.

20 Additionally, ALA appears to possess a dual action related to hunger and  $\beta$ -oxidation of fat. First, the activity of AMP-activated protein kinase, which acts as an energy sensor in the hypothalamus, is reduced by ALA in rodents, this results in a profound weight loss by reducing food intake and enhancing energy

expenditure (Kim MS, Park JY, Namkoong C, Jang PG, Ryu JW, Song HS, Yun JY, Namgoong IS, Ha J, Park IS, Lee IK, Viollet B, Youn JH, Lee HK, Lee KU. Anti-obesity effects of alpha-lipoic acid mediated by suppression of hypothalamic AMP-activated protein kinase. *Nat Med.* 2004 Jul;10(7):727-33). Second, ALA increases Uncoupling Protein-1 in rodent adipocytes while increasing AMP-activated protein kinase in skeletal muscle cells and increasing glucose uptake and energy expenditure (Lee WJ, Koh EH, Won JC, Kim MS, Park JY, Lee KU. Obesity: the role of hypothalamic AMP-activated protein kinase in body weight regulation. *Int J Biochem Cell Biol.* 2005 Nov;37(11):2254-9). Therefore, ALA seemingly has different effects in different tissues. However, in adipocytes or muscle cells ALA increases fatty acid oxidation, leading to an increase in energy expenditure and a decrease in weight and food intake.

U.S. Patent Nos. 6,136,339 and 6,620,425 disclose compositions and methods for enhancing an athlete's muscle size or strength using a combination of Creatine, Alpha Lipoic Acid and optionally Dextrose, to be taken mixed with water daily following exercise.

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Alpha Lipoic Acid or derivatives thereof. A serving of the dietary supplement may include from about 0.005 g to about 0.4 g of Alpha Lipoic Acid or derivatives thereof. The preferred dosage of a serving of the dietary supplement comprises about 0.25 g of Alpha Lipoic Acid or derivatives thereof.

**Dextrose**

Dextrose is a simple sugar or monosaccharide commonly known as D-glucose. Also known as 'grape sugar' or 'blood sugar', it is found mainly in honey and fruits and is a building-block of glycogen, cellulose and starch. Recently,  
5 Dextrose was shown to boost the performance a female rowers as compared to ribose, which had been theorized to replenish muscle energy (Dunne L, Worley S, Macknin M. Ribose versus dextrose supplementation, association with rowing performance: a double-blind study. Clin J Sport Med. 2006 Jan;16(1):68-71).

In an embodiment of the present invention, which is set forth in greater  
10 detail in the examples below, the dietary supplement may include Dextrose. A serving of the dietary supplement may include from about 50 g to about 100 g of Dextrose. The preferred dosage of a serving of the dietary supplement comprises about 75 g of Dextrose.

**Mulberry extract**

15 Mulberry (*Morus alba*) is an edible plant used in Chinese medicine which is rich in flavonoids possessing antioxidant activity (Doi K, Kojima T, Makino M, Kimura Y, Fujimoto Y. Studies on the constituents of the leaves of *Morus alba* L. Chem Pharm Bull (Tokyo). 2001 Feb;49(2):151-3). Orally administered mulberry extracts of Mulberry reduced blood glucose levels of both non-diabetic and  
20 streptozotocin-treated diabetic rats, commensurate with decreased food intake (Musabayane CT, Bwititi PT, Ojewole JA. Effects of oral administration of some herbal extracts on food consumption and blood glucose levels in normal and streptozotocin-treated diabetic rats. Methods Find Exp Clin Pharmacol. 2006

May;28(4):223-8). Orally consumed extracts of Mulberry have also been shown to inhibit increases in blood glucose resulting from the ingestion of carbohydrates such as sucrose in humans and rats (Oku T, Yamada M, Nakamura M, Sadamori N, Nakamura S. Inhibitory effects of extractives from leaves of *Morus alba* on human and rat small intestinal disaccharidase activity. *Br J Nutr.* 2006 May;95(5):933-8). Furthermore, extracts of Mulberry confer neuroprotective benefits (Kang TH, Oh HR, Jung SM, Ryu JH, Park MW, Park YK, Kim SY. Enhancement of neuroprotection of mulberry leaves (*Morus alba* L.) prepared by the anaerobic treatment against ischemic damage. *Biol Pharm Bull.* 2006 Feb;29(2):270-4) and may further attenuate the development of atherosclerotic lesions (Enkhmaa B, Shiwaku K, Katsube T, Kitajima K, Anuurad E, Yamasaki M, Yamane Y. Mulberry (*Morus alba* L.) leaves and their major flavonol quercetin 3-(6-malonylglucoside) attenuate atherosclerotic lesion development in LDL receptor-deficient mice. *J Nutr.* 2005 Apr;135(4):729-34).

15 In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Mulberry extract. A serving of the dietary supplement may include from about 0.01 g to about 0.05 g of Mulberry extract. The preferred dosage of a serving of the dietary supplement comprises about 0.025 g of Mulberry extract.

## 20 **Chromium**

Chromium is an essential trace mineral that is used to control blood sugar levels by aiding insulin, which can help control or reduce weight. Chromium is poorly absorbed by the body and must therefore be combined with a more

efficiently absorbed compound such as niacin as in the case of polynicotinate. Chromium likely exerts its main function as a component or a co-factor of the glucose tolerance factor, which is involved in insulin sensitivity.

Chromium has been shown clinically to increase lean mass (Bahadori B, Wallner S, Schneider H, Wascher TC, Toplak H. Effect of chromium yeast and chromium picolinate on body composition of obese, non-diabetic patients during and after a formula diet. *Acta Med Austriaca*. 1997;24(5):185-7) and reduce body fat when combined with exercise (Grant KE, Chandler RM, Castle AL, Ivy JL. Chromium and exercise training: effect on obese women. *Med Sci Sports Exerc*. 1997 Aug;29(8):992-8). Moreover, chromium has also been shown to increase high density lipoproteins (HDL i.e. 'good' cholesterol) (Riales R, Albrink MJ. Effect of chromium chloride supplementation on glucose tolerance and serum lipids including high-density lipoprotein of adult men. *Am J Clin Nutr* 1981;34:2670-8). Numerous clinical studies have demonstrated the relationship between supplemental Chromium and improved insulin activity and glucose metabolism (Anderson RA. Chromium in the prevention and control of diabetes. *Diabetes Metab*. 2000 Feb;26(1):22-7).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include a derivative of Chromium. A serving of the dietary supplement may include from about 0.001 g to about 0.005 g of a derivative of Chromium. The preferred dosage of a serving of the dietary supplement comprises about 0.003 g of a derivative of Chromium.

## Glutamine

Glutamine is the most abundant amino acid found in muscle and has important functions as a precursor for the synthesis of other amino acids. Many cells required for immune function rely on Glutamine as source for energy  
5 production.

Physical activity can deplete Glutamine levels, and as such, Glutamine is often considered to be a 'conditionally essential' amino acid. A study examining the Glutamine levels of groups involved in several different types of activities or sports found that powerlifters and swimmers had lower Glutamine levels than  
10 cyclists and non-athletes (Hiscock N, Mackinnon LT. A comparison of plasma glutamine concentration in athletes from different sports. *Med Sci Sports Exerc.* 1998 Dec;30(12):1693-6), suggesting that high resistance load activities require increased amounts of Glutamine. Moreover, this depletion of Glutamine has been linked to immunosuppression often resulting from intense training  
15 (Newsholme EA. Biochemical mechanisms to explain immunosuppression in well-trained and overtrained athletes. *Int J Sports Med.* 1994 Oct;15 Suppl 3:S142-7). Supplementation with Glutamine in conjunction with additional antioxidants can increase body weight, body cell mass, and intracellular water when compared with placebo (Shabert JK, Winslow C, Lacey JM, Wilmore DW. Glutamine-antioxidant supplementation increases body cell mass in AIDS  
20 patients with weight loss: a randomized, double-blind controlled trial. *Nutrition.* 1999 Nov-Dec;15(11-12):860-4). Glutamine is also capable of stimulating insulin secretion (Tanizawa Y, Nakai K, Sasaki T, Anno T, Ohta Y, Inoue H, Matsuo K,

Koga M, Furukawa S, Oka Y. Unregulated elevation of glutamate dehydrogenase activity induces glutamine-stimulated insulin secretion: identification and characterization of a GLUD1 gene mutation and insulin secretion studies with MIN6 cells overexpressing the mutant glutamate dehydrogenase. *Diabetes*. 2002 Mar;51(3):712-7).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Glutamine or a derivative thereof. A serving of the dietary supplement may include from about 0.001 g to about 0.005 g of Glutamine or a derivative thereof. The preferred dosage of a serving of the dietary supplement comprises about 0.002 g of Glutamine or a derivative thereof.

#### **Enicostemma littorale Blume**

*Enicostemma littorale Blume* is a flower-producing herb found in South America, Africa, and Asia. In rat models of diabetes, *Enicostemma littorale* extract can enhance glucose-induced insulin release thereby effectively lowering blood glucose levels (Maroo J, Vasu VT, Aalinkeel R, Gupta S. Glucose lowering effect of aqueous extract of *Enicostemma littorale* Blume in diabetes: a possible mechanism of action. *J Ethnopharmacol*. 2002 Aug;81(3):317-20; Maroo J, Vasu VT, Gupta S. Dose dependent hypoglycemic effect of aqueous extract of *Enicostemma littorale blume* in alloxan induced diabetic rats. *Phytomedicine*. 2003 Mar;10(2-3):196-9). Furthermore, *Enicostemma littorale* extract counters the changes in several metabolic enzymes and antioxidants observed in diabetic rats, including lowering thiobarbituric acid reactive substances and lipid



hydroperoxides while increasing the concentration of reduced glutathione and the activities of superoxide dismutase and catalase (Srinivasan M, Padmanabhan M, Prince PS. Effect of aqueous *Enicostemma littorale* Blume extract on key carbohydrate metabolic enzymes, lipid peroxides and antioxidants in alloxan-  
 5 induced diabetic rats. J Pharm Pharmacol. 2005 Apr;57(4):497-503). The lipid profile of rats fed cholesterol was also improved by administration of *Enicostemma littorale* extract (Vasu VT, Modi H, Thaikoottathil JV, Gupta S. Hypolipidaemic and antioxidant effect of *Enicostemma littorale* Blume aqueous extract in cholesterol fed rats. J Ethnopharmacol. 2005 Oct 3;101(1-3):277-82).

10 In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include *Enicostemma littorale* Blume. A serving of the dietary supplement may include from about 0.0005 g to about 0.003 g of *Enicostemma littorale* Blume. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of *Enicostemma*  
 15 *littorale* Blume.

### **Scoparia dulcis (Scotch brum)**

*Scoparia dulcis* is a tropical herb found in abundance in South America and the Amazon rainforest and has been used traditionally for multiple treatments including diabetes. Extracts of *Scoparia dulcis* provide both  
 20 antidiabetic and antihyperlipidemic actions in normal and experimentally diabetic rats (Pari L, Latha M. Antihyperlipidemic effect of *Scoparia dulcis* (sweet broomweed) in streptozotocin diabetic rats. J Med Food. 2006 Spring;9(1):102-7). *Scoparia dulcis* extract has also demonstrated antioxidant and

neuroprotective activity (Pari L, Latha M. Protective role of *Scoparia dulcis* plant extract on brain antioxidant status and lipidperoxidation in STZ diabetic male Wistar rats. BMC Complement Altern Med. 2004 Nov 2;4:16).

In an embodiment of the present invention, which is set forth in greater  
5 detail in the examples below, the dietary supplement may include *Scoparia dulcis*. A serving of the dietary supplement may include from about 0.0005 g to about 0.003 g of *Scoparia dulcis*. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of *Scoparia dulcis*.

#### **Tarragon extract (*Artemisia dracunculus*)**

10 Russian Tarragon (*Artemisia dracunculus*) is a perennial herb widely used in cooking. Historically, it has been used as a natural blood cleanser and as a treatment for headaches and dizziness. Current studies are examining the use of an ethanolic extract of Russian Tarragon for the treatment of hyperglycemia associated with diabetes. The toxicology of this extract has been evaluated, and  
15 has been shown to be safe and non-toxic (Ribnicky DM, Poulev A, O'Neal J, Wnorowski G, Malek DE, Jager R, Raskin I. Toxicological evaluation of the ethanolic extract of *Artemisia dracunculus* L. for use as a dietary supplement and in functional foods. Food Chem Toxicol. 2004 Apr;42(4):585-98). Essential oil extracted from *Artemisia dracunculus* may also have potential as an  
20 anticonvulsant and as a mild sedative (Sayyah M, Nadjafnia L, Kamalinejad M. Anticonvulsant activity and chemical composition of *Artemisia dracunculus* L. essential oil. J Ethnopharmacol. 2004 Oct;94(2-3):283-7).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Tarragon extract. A serving of the dietary supplement may include from about 0.0005 g to about 0.003 g of Tarragon extract. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of Tarragon extract.

### **Andrographis paniculata**

*Andrographis paniculata* is a medicinal herb used traditionally throughout Asia used to treat a number of conditions. Clinical studies have demonstrated an immunity-enhancing benefit of *Andrographis paniculata* supplementation by reducing the occurrence and severity of common cold symptoms (Caceres DD, Hancke JL, Burgos RA, Sandberg F, Wikman GK. Use of visual analogue scale measurements (VAS) to assess the effectiveness of standardized *Andrographis paniculata* extract SHA-10 in reducing the symptoms of common cold. A randomized double blind-placebo study. *Phytomedicine*. 1999 Oct;6(4):217-23) and upper-respiratory tract infections (Melchior J, Spasov AA, Ostrovskij OV, Bulanov AE, Wikman G. Double-blind, placebo-controlled pilot and phase III study of activity of standardized *Andrographis paniculata* Herba Nees extract fixed combination (Kan jang) in the treatment of uncomplicated upper-respiratory tract infection. *Phytomedicine*. 2000 Oct;7(5):341-50). Additionally, *Andrographis paniculata* has been shown to possess antipyretic, fever-reducing, activity similar to that of aspirin (Vedavathy S, Rao KN. Antipyretic activity of six indigenous medicinal plants of Tirumala Hills, Andhra Pradesh, India. *J Ethnopharmacol*. 1991 May-Jun;33(1-2):193-6). Furthermore, *Andrographis paniculata* has been

shown to reduce chemically-induced liver toxicity in experimental mice (Kapil A, Koul IB, Banerjee SK, Gupta BD. Antihepatotoxic effects of major diterpenoid constituents of *Andrographis paniculata*. *Biochem Pharmacol*. 1993 Jul 6;46(1):182-5).

5            *Andrographis paniculata* extract possesses antihyperglycemic and antioxidative activities in both normal and chemically-induced diabetic rats (Zhang XF, Tan BK. Antihyperglycaemic and anti-oxidant properties of *Andrographis paniculata* in normal and diabetic rats. *Clin Exp Pharmacol Physiol*. 2000 May-Jun;27(5-6):358-63). The antidiabetic properties of *Andrographis*  
10 *paniculata* are believed to be due at least in part to enhanced glucose metabolism (Zhang XF, Tan BK. Anti-diabetic property of ethanolic extract of *Andrographis paniculata* in streptozotocin-diabetic rats. *Acta Pharmacol Sin*. 2000 Dec;21(12):1157-64).

In an embodiment of the present invention, which is set forth in greater  
15 detail in the examples below, the dietary supplement may include *Andrographis paniculata*. A serving of the dietary supplement may include from about 0.0005 g to about 0.003 g of *Andrographis paniculata*. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of *Andrographis paniculata*.

#### **Double Fermented Triticum aestivum**

20            Double Fermented Triticum aestivum is a whole-grain wheat product low in simple sugars and high in complex carbohydrates. This produces a more level glucose/insulin response rather than the typical 'spike' resulting from simple sugar ingestion. As such, Double Fermented Triticum aestivum is marketed

towards overweight or obese individual or individuals with impaired glucose tolerance. Double Fermented Triticum aestivum was found effective at reducing the risks associated with development of type 2 diabetes such as elevated fasting blood glucose levels and obesity (Rave K, Dellweg S, Hovelmann U, Heise T, Dieck HT. Impact of a Diet with Balantose™ on Insulin Resistance, Lipids and Body Weight: Results of a Randomized, Controlled Cross-Over Study in Obese Subjects with High Risk for Type 2 Diabetes. 65<sup>th</sup> Annual Scientific Sessions, American Diabetes Association 2005, Abstract 1765-P).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Double Fermented Triticum aestivum. A serving of the dietary supplement may include from about 0.05 g to about 0.3 g of Double Fermented Triticum aestivum. The preferred dosage of a serving of the dietary supplement comprises about 0.1 g of Double Fermented Triticum aestivum.

#### 15 **Isomalt**

Isomalt is a disaccharide sugar substitute derived from sucrose which is less sweet than, and is often mixed with, more conventional sweeteners. Being only partially digested in the intestines, isomalt results in a low blood glucose effect, has benefits similar to that of dietary fiber, and has a caloric value of about half that of sugar. Moreover, Isomalt has been shown to promote healthy bowel function without impairing metabolic function (Gostner A, Schaffer V, Theis S, Menzel T, Luhrs H, Melcher R, Schauber J, Kudlich T, Dusel G, Dorbath D, Kozianowski G, Scheppach W. Effects of isomalt consumption on gastrointestinal

and metabolic parameters in healthy volunteers. Br J Nutr. 2005 Oct;94(4):575-81; Gostner A, Blaut M, Schaffer V, Kozianowski G, Theis S, Klingeberg M, Dombrowski Y, Martin D, Ehrhardt S, Taras D, Schwiertz A, Kleessen B, Luhrs H, Schauber J, Dorbath D, Menzel T, Scheppach W. Effect of isomalt consumption on faecal microflora and colonic metabolism in healthy volunteers. Br J Nutr. 2006 Jan;95(1):40-50).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Isomalt. A serving of the dietary supplement may include from about 0.0005 g to about 0.003 g of Isomalt. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of Isomalt.

### **Trehalose**

Trehalose is a naturally occurring disaccharide found in plants, invertebrates and fungi and is about half as sweet as sucrose or table sugar. Trehalose has been discovered to be able to inhibit the aggregation of some proteins and thus has potential in the prevention of diseases linked to such events such as Huntington's disease (Tanaka M, Machida Y, Niu S, Ikeda T, Jana NR, Doi H, Kurosawa M, Nekooki M, Nukina N. Trehalose alleviates polyglutamine-mediated pathology in a mouse model of Huntington disease. Nat Med. 2004 Feb;10(2):148-54).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include Trehalose. A serving of the dietary supplement may include from about 0.0005 g to about

0.003 g of Trehalose. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of Trehalose.

### **D-Mannose**

Mannose is a monosaccharide found in some fruits including cranberry. It is absorbed slowly in the gastrointestinal tract, with most being excreted in the urine. D-mannose has been theorized to aid in the treatment of urinary tract infections by virtue of being able to bind to the surface proteins of infection-causing bacteria, thereby facilitating their clearance (Schaeffer AJ, Chmiel JS, Duncan JL, Falkowski WS. Mannose-sensitive adherence of Escherichia coli to epithelial cells from women with recurrent urinary tract infections. J Urol. 1984 May;131(5):906-10).

In an embodiment of the present invention, which is set forth in greater detail in the examples below, the dietary supplement may include D-mannose. A serving of the dietary supplement may include from about 0.0005 g to about 0.003 g of D-mannose. The preferred dosage of a serving of the dietary supplement comprises about 0.001 g of D-mannose.

According to various embodiments of the present invention, the dietary supplement may be consumed in any form. For instance, the dosage form of the dietary supplement may be provided as, e.g., a powder beverage mix, a liquid beverage, a ready-to-eat bar or drink product, a capsule, a liquid capsule, a tablet, a caplet, or as a dietary gel. The preferred dosage forms of the present invention is as a powder beverage mix or a drink product.

### **Fine-milling of Active Constituents**

As set forth above, the dosage form of the dietary supplement, in accordance with the example embodiments set forth below, may be provided in accordance with customary processing techniques for herbal and/or dietary supplements, wherein the active ingredients are suitably processed into a desired form. In accordance with various embodiments of the present invention, one or more ingredients of the diet supplement are processed so as to form fine-milled particles. For instance, in various embodiments, one or more ingredients of the dietary supplemental are processed by a large-scale dry milling technique that produces fine particles, preferably known as fine-milled particles. The use of dry milling techniques, in combination with excipients and polymers, to form fine-milled particles has been shown to improve flow and dispersability, stability, resistance to moisture, bioavailability, and dissolution/release properties. Formulations benefit by containing fine-milled particles for the purpose of providing the one or more ingredients in particle sizes that optimize one or more of the flow and dispersability, stability, resistance to moisture, bioavailability, and dissolution/release properties of the one or more ingredients in a dietary supplement. *In vitro* tests designed to simulate the environment of a stomach were performed to test the dissolution rate of fine-milled particle tablets versus non-fine-milled. These test showed that in tablets produced from fine-milled particles the time to 100% dissolution was approximately 15 minutes. In the case of non-fine-milled particle compositions, only 90% dissolution was observed after 120 minutes. In preferred embodiments, the dietary supplemental contains fine-



milled particles having an average size between about 50 nm and about 2 nm.

U.S. Provisional Patent Application 60/776,325 discloses a method for improving the absorption, palatability, taste, texture, and bioavailability of compounds by increasing the solubility of said compounds in proprietary  
5 formulations for the purposes of enhancing or improving muscle size, growth and/or recovery time and/or weight loss. The increased bioavailability of the compound or ingredients is achieved by reducing the particle size via “fine-milling” thereby increasing the surface area-to-volume ratio each particle, thus increasing the rate of dissolution. The compositions and methods disclosed  
10 promote increased bioavailability by increasing the total surface area of poorly soluble particles, thereby increasing the rate of absorption.

As used herein the, term “fine-milled” and/or “fine-milling” refers to the process of micronization. Micronization is a mechanical process that involves the application of force to a particle, thereby resulting in a reduction in the size of the  
15 particle. The force, in the case of micronization, may be applied in any manner such as, e.g., the collision of particles at high rates of speed, grinding, or by an air-jet micronizer. In preferred embodiments, fine-milled particles are obtained by jet-milling with nitrogen and compressed air.

As used herein, the term “particle size” refers to the diameter of the  
20 particle. The term “average particle size” means that at least 50% of the particles in a sample will have the specified particle size. Preferably, at least 80% of the particles in a sample will have the specified particle size, and more preferably, at least 90% of the particles in a given sample will have the specified particle size.

The size of a particle can be determined by any of the methods known within the art. Methods for particle size determination which may be employed are for example, e.g., sieves, sedimentation, electrozone sensing (Coulter counter), microscopy, and/or Low Angle Laser Light Scattering. The preferred  
5 methods for the particle size determination of the present invention are those methods which are most commonly used in the pharmaceutical industry, such as laser diffraction, e.g., via light scattering Coulter Delsa 440SX.

The fine-milling process may be employed in the processing of one or more of the ingredients of the present invention in the dosage forms of tablets,  
10 e.g., immediate-release film coated, modified-release and fast-dissolving; capsules or tablets, e.g., immediate-release and modified-release; liquid dispersions; powders; drink mixes, etc.

Preferably, the dietary supplement of the present invention is consumed by an individual in accordance with the following method: As a dietary  
15 supplement, a serving of said dietary supplement may be taken by means of mixing in about 360-450ml of an acceptable aqueous fluid at least one (1) time daily wherein each serving is comprised of two (2) scoops comprising about 100g total mass of the dietary supplement. Said dietary supplement may be consumed approximately 0 to 60 minutes following a workout, or in the morning upon  
20 waking on non-workout days. In this manner, the dietary supplement may increase Creatine uptake and retention in skeletal muscle, increase muscle mass and strength, increase exercise capacity and aid in post-exercise recovery as

well as provide support for the immune system during intense exercise training periods.

Furthermore, the dosage form of the supplemental composition may be provided in accordance with customary processing techniques for herbal and dietary supplements in any of the forms mentioned above. Additionally, the dietary supplement set forth in the example embodiments herein may contain any appropriate number and type of excipients, as is well-known in the art.

The present dietary supplement or those similarly envisioned by one of skill in the art, may be utilized in compositions and methods for increasing Creatine uptake and retention in skeletal muscle, increasing muscle mass and strength, increasing exercise capacity and aiding in post-exercise recovery as well as providing support for the immune system during intense exercise training periods of an individual, e.g. a human or an animal in a formulation designed to be consumed at least one time per day.

Although the following examples illustrate the practice of the present invention in three of its various embodiments, the examples should not be construed as limiting the scope of the invention. Other embodiments will be apparent to one skilled in the art from consideration of the specification and example.

**Example 1**

A serving of the dietary supplement comprises the following ingredients in powdered beverage mix form. The dietary supplement comprises for example: about 74 g of pharma grade Dextrose 99 DE, about 9 g of Creatine monohydrate, 5 finely ground or milled, about 2.1 g of Taurine, about 0.33 g of Dipotassium Phosphate, about 0.33 g of Magnesium Phosphate, about 0.26 g of Sodium Alpha Lipoic Acid, about 0.025 g of and extract of Mulberry, about 0.003 g of Chromium polynicotinate, about 0.001 g of Anhydrous Creatine, about 0.001 g of Taurine ethyl ester HCl, about 0.001 g of Glutamine AKG 2:1, about 0.001 g of 10 Glutamine ethyl ester HCl, about 0.001 g of *Enicostemma littorale Blume*, about 0.001 g of *Scoparia dulcis*, about 0.001 g of an extract of Tarragon, about 0.001 g of *Andrographis paniculata*.

**Directions:** As a dietary supplement, 2 scoops, comprising about 100g total mass of the dietary supplement are administered by a means of mixing said 15 dietary supplement in 360-450ml of an acceptable aqueous fluid at least one (1) time daily. Said serving is to be consumed approximately 0 to 60 minutes following a workout or in the morning upon waking on non-workout days.

**Example 2**

A serving of the dietary supplement comprises the following ingredients in powdered beverage mix form. The dietary supplement comprises for example: about 75 g of pharma grade Dextrose 99 DE, about 9 g of finely ground Creatine monohydrate, about 2.1 g of Taurine, about 1 g of fine-milled Creatine monohydrate, about 0.33 g of Dipotassium Phosphate, about 0.33 g of Disodium Phosphate, about 0.26 g of the Sodium salt of Alpha Lipoic Acid, about 0.025 g of an extract of Mulberry, about 0.003 g of Chromium polynicotinate, about 0.001 g of Anhydrous Creatine, about 0.001 g of Dicreatine malate, about 0.001 g of Creatine HCA salt, about 0.001 g of Taurine ethyl ester HCl, about 0.001 g of Glutamine AKG 2:1, about 0.001 g of Glutamine ethyl ester HCl, about 0.001 g of *Enicostemma littorale Blume*, about 0.001 g of *Scoparia dulcis*, about 0.001 g of an extract of Tarragon extract, and about 0.001 g of *Andrographis paniculata*.

**Directions:** As a dietary supplement, 2 scoops, comprising about 100g total mass of the dietary supplement are administered by a means of mixing said dietary supplement in 360-450ml of an acceptable aqueous fluid at least one (1) time daily. Said serving is to be consumed approximately 0 to 60 minutes following a workout or in the morning upon waking on non-workout days.

**Example 3**

A serving of the dietary supplement comprises the following ingredients in powdered beverage mix form. The dietary supplement comprises for example: about 75 g of pharma grade Dextrose 99 DE, about 9 g of finely ground Creatine monohydrate, about 2.1 g of Taurine, about 1 g of fine-milled Creatine monohydrate, about 0.33 g of Dipotassium Phosphate, about 0.33 g of Disodium Phosphate, about 0.33 g of Magnesium Phosphate, about 0.26 g of Sodium Alpha Lipoic Acid, about 0.1 g of Double Fermented Triticum aestivum, about 0.025 g of an extract of Mulberry, about 0.003 g of Chromium polynicotinate, about 0.001 g of Anhydrous Creatine, about 0.001 g of Creatine Dicreatine malate, about 0.001 g of Creatine pyroglutamate, about 0.001 g of Creatine HCA salt, about 0.001 g of Taurine ethyl ester HCl, about 0.001 g of Glutamine AKG 2:1, about 0.001 g of Glutamine ethyl ester HCl, about 0.001 g of *Enicostemma littorale Blume*, about 0.001 g of *Scoparia dulcis*, about 0.001 g of and extract of Tarragon, about 0.001 g of *Andrographis paniculata*, about 0.001 g of Isomalt, about 0.001 g of Trehalose ,about 0.001 g of D-mannose.

**Directions:** As a dietary supplement, 2 scoops, comprising about 100g total mass of the dietary supplement are administered by a means of mixing said dietary supplement in 360-450ml of an acceptable aqueous fluid at least one (1) time daily. Said serving is to be consumed approximately 0 to 60 minutes following a workout or in the morning upon waking on non-workout days.

In the foregoing specification, the invention has been described with specific embodiments thereof, however, it will be evident that various modifications and changes may be made thereto without departing from the broader spirit and scope of the invention.

**What is claimed:**

1. A dietary supplement comprising at least a combination of Creatine or derivative thereof, Taurine or derivative thereof and a source of Phosphate.
- 5 2. The dietary supplement of claim 1, wherein said source of Phosphate is selected from the list of Dipotassium Phosphate, Disodium Phosphate, Magnesium Phosphate.
3. The dietary supplement of claim 1, further comprising at least one of  
10 Double Fermented Triticum aestivum, Trehalose, and Isomaltose.
4. The dietary supplement of claim 1, further comprising at least one of an extract of Mulberry, Enciostemma Littorale Blume, Scoparia Dulcis, and extract of Tarragon, Andrographis Paniculata, and a derivative of Chromium.  
15
5. The dietary supplement of claim 1, further comprising at least one of Andrographis Paniculata, and Glutamine.
6. The dietary supplement of claim 1, further comprising at least one of Alpha  
20 Lipoic Acid and an extract of Mulberry.
7. A method of increasing the energy stores in a muscle and prolonging the ability of a muscle to perform work comprising the step of administering to an



individual a dietary supplement comprising Creatine or derivative thereof, Taurine or derivative thereof and a source of Phosphate.

8. The method of claim 7, wherein said source of Phosphate is selected from  
5 the list of Dipotassium Phosphate, Disodium Phosphate, Magnesium Phosphate.

9. The method of claim 8, wherein the dietary supplement further comprises  
at least one of Double Fermented Triticum aestivum, Dextrose, Trehalose, and  
Isomaltose.  
10

10. The method of claim 9, wherein the ingredients of the dietary supplement  
are provided in amounts suitable to increase muscular Creatine retention in an  
individual.

15 11. The method claim 8, wherein the dietary supplement further comprises at  
least one of an extract of Mulberry, Enciostemma Littorale Blume, Scoparia  
Dulcis, and extract of Tarragon, Andrographis Paniculata, and a derivative of  
Chromium.

20 12. The method of claim 11, wherein the ingredients of the dietary supplement  
are provided in amounts suitable to maintain a blood sugar level plateau in an  
individual in order maintain insulin secretion.

13. The method of claim 8, wherein the dietary supplement further comprises Andrographis Paniculata, and Glutamine.

14. The method of claim 13, wherein the ingredients of the dietary supplement are provided in amounts suitable to support the immune system in an individual during intense bouts of physical training.

15. The method of claim 8, wherein the dietary supplement further comprises at least one of Alpha Lipoic Acid and an extract of Mulberry.

10

16. The method of claim 15, wherein the ingredients of the dietary supplement are provided in amounts suitable to reduce food intake leading to fat loss and weight loss.

15 17. The method of claim 15, wherein the ingredients of the dietary supplement are provided in amounts suitable to supply antioxidant to an individual.

18. A dietary supplement comprising:

about 10 g of Creatine or derivative thereof;

20

about 2.1 g of Taurine or derivative thereof;

about 0.5 g of an acceptable a Phosphate donor;

about 0.1 g of Double Fermented Triticum aestivum;

about 82 g of Dextrose;

about 0.001 g of Trehalose;

about 0.001 g of Isomaltose;

about 0.025 g of an extract of Mulberry;

about 0.001 g of Enciostemma Littorale Blume;

5 about 0.001 g of Scoparia Dulcis;

about 0.001 g of and extract of Tarragon;

about 0.001 g of Andrographis Paniculata;

about 0.0003 g of a derivative of Chromium Polynicotinate;

about 0.002 g of Glutamine;

10 about 0.25 g of Alpha Lipoic Acid.