CREATINE ORAL SUPPLEMENTATION USING CREATINE HYDROCHLORIDE SALT

CROSS-REFERENCE TO RELATED APPLICATIONS

This is a divisional of U.S. Patent Application No. 12/909,377, filed October 21, 2012, now U.S. Patent No. 8,354,450, which is a continuation-in-part of U.S. Patent Application No. 12/477,413, filed June 3, 2009, now U.S. Patent No. 8,026,385, which is a continuation of U.S. Patent Application No. 10/846,782, filed May 14, 2004, now U.S. Patent No. 7,608,641, which claims priority to U.S. Provisional Application 60/470,356, filed May 15, 2003, the entirety of which is incorporated herein.

FIELD OF THE INVENTION

The present invention is directed to a form of creatine that has increased aqueous solubility, increased plasma uptake at low dosage amounts, and improved stability and half-life. In particular, the present invention relates to a creatine supplement that, when compared to creatine monohydrate, has an increased aqueous solubility of at least an order of magnitude, a bioavailability or plasma uptake level of at least 50 percent greater than creatine monohydrate, and a shelf-life of more than double the shelf-life of creatine monohydrate.

BACKGROUND OF THE INVENTION

Creatine is a naturally occurring nitrogenous compound found in the skeletal muscles of vertebrates that plays an important role in protein metabolism and other bio-chemical functions. For example, creatine is taken up into muscle cells by specific receptors and converted to phosphocreatine by creatine kinase.

Both creatine and phosphocreatine play an important role in the anaerobic production of ATP during short and intensive exertions, via the creatine kinase system. Specifically, during muscle contraction, there is an increase in the amount of phosphocreatine (which is generated from creatine) and consequently in ATP. The amount of phosphocreatine in the muscle cell determines the amount of time it takes for a muscle to recover from activity; thus, supplementing the diet with creatine can increase

the concentration of phosphocreatine in muscles by 6 percent to 16 percent, with a consequent increase in the ATP turnover during physical exertion.

Creatine-containing supplements have been shown to increase lean body mass, high intensity power output, and overall physical strength. By virtue of these characteristics, creatine has met with enormous success among professional and recreational athletes, as well as professional and amateur bodybuilders, in recent years as a dietary supplement.

Increasing creatine levels in muscle through dietary supplementation has proven effective at enhancing athletic performance, increasing muscle workload and shortening muscle recovery time. In addition, there is increasing interest in creatine dietary supplements for a variety of therapeutic indications, including muscular dystrophy, cardiovascular diseases, neurodegenerative disorders, and mental retardation. The zwitterionic creatine monohydrate has been the standard creatine salt of choice for commercial creatine supplement formulations.

However, creatine supplements containing creatine monohydrate are not ideal dietary supplements due to their low aqueous solubility. In other words, relatively large doses of creatine monohydrate must be consumed with large amounts of fluid for effective use. People often experience excessive water retention (bloating), cramps, and significant gastrointestinal problems due to the large dosages. In addition, the relatively high doses of creatine monohydrate required to produce the desired biological effects suggest that the oral bioavailability of creatine monohydrate is low and that more efficient dosage forms may provide better desired results accompanied by fewer gastrointestinal side effects.

There are other known salt forms of creatine including creatine citrate (creatine effervescent) and creatine pyruvate that have been patented and marketed as improvements over creatine monohydrate. However, despite the various salt forms currently marketed, there remains a need in the art for a more improved form of creatine with improved solubility and bioavailability characteristics that can be consumed in smaller dosage forms.

SUMMARY OF THE INVENTION

The present invention is directed to a supplement that includes creatine HCl, wherein the creatine HCl possesses a solubility of at least 600 mg/mL in water at 25°C. In one embodiment, the creatine HCl is at least 95 percent free of contaminants. In another embodiment, the recommended dosage range for the creatine HCl is between about one quarter teaspoon to about one tablespoon per hundred pounds body weight.

In this aspect of the invention, the supplement may be being taken orally. In one embodiment, the creatine HCl has a shelf-life of at least about 45 days in aqueous solution at room temperature. In another embodiment, an effective dosage of the supplement is about 500 mg to about 1500 mg of creatine HCl per 100 pounds body weight. In yet another embodiment, the creatine HCl further comprises an additive or feed supplement for livestock.

The present invention is also directed to a formula used to enhance athletic performance including creatine HCl, wherein the creatine HCl exhibits an aqueous solubility that is at least about 15 times greater than that of creatine monohydrate. In one embodiment, the formula also includes additional species of creatine selected from the group comprising creatine esters, creatine pyruvate, creatine phosphate, creatine alpha-ketoglutarate, creatine citrate, and combinations thereof. In another embodiment, the formula also includes additional supplements selected from the group comprising carbonate salts, methylsulfonylmethane, glucosamine, and chondroitin.

In yet another embodiment, the formula also includes compounds selected from the group comprising proteins, amino acid supplements, carbohydrates, D-Ribose, fats, fiber and combinations thereof. In still another embodiment, the formula also includes sweeteners selected from the group comprising sucralose, aspartame, saccharin, acesulfame potassium, neohesperidin dihydrochalcone, glycyrrhizin, thaumatin, alitame, stevioside, and combinations thereof. In one embodiment, the formula further includes a supplement selected from the group comprising sports bars, nutritional bars, powders, liquids, gels, sports drinks, and beverages. In another embodiment, the formula also includes flavoring agents selected from the group comprising cocoa, yogurt, peanut butter, mint, cheesecake, hazelnut paste, almonds, granola, coconut, strawberry, banana,

cherry, plum, raspberry, lemon, orange, lime, pineapple, blueberry and other fruit flavors, coffee, or cremes and jellies, and combinations thereof.

The present invention is also directed to a granular powder including a creatine HCl product formed by the reaction of an alcohol, an acid catalyst, and creatine monohydrate, wherein the solubility of the creatine HCl product is at least about 650 mg/ml.

In this aspect of the invention, the alcohol may be selected from the group consisting of ethanol, methanol, butanol, and isopropanol. In one embodiment, the reaction is a super-saturated reaction including ethanol, acetyl chloride, and creatine monohydrate. In one embodiment, the volume of ethanol used is between about 4 and 5 L per kg of creatine monohydrate and the quantity of acetyl chloride used is between about 1.0 to about 1.1 mole equivalents of creatine monohydrate.

In another embodiment, the super-saturated reaction further includes the steps of mixing the alcohol and acetyl chloride in a reactor that is cooled to between about 0 °C and 20 °C; allowing the temperature of the reactor to increase to about 38 °C; adding creatine monohydrate; and maintaining a temperature of between about 30 °C and about 40 °C. The creatine HCl product is preferably at least 95 percent free of contaminants.

BRIEF DESCRIPTION OF THE DRAWINGS

Further features and advantages of the invention can be ascertained from the following detailed description that is provided in connection with the drawing(s) described below:

FIG. 1 is a graphical representation in linear form of the stability of creatine HCl in aqueous solution as compared to creatine monohydrate; and

FIG. 2 is a graphical representation in log form of the stability of creatine HCl in aqueous solution as compared to creatine monohydrate.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed to a third generation form of creatine, specifically a creatine hydrochloride salt ("creatine HCl") that has improved aqueous solubility, plasma uptake, and shelf-life over that of previous forms of creatine. The

present invention further contemplates suitable methods to produce the creatine HCl in a granular precipitate form with high purity and yield.

The creatine HCl of the present invention may be used as a nutritional supplement for enhancing muscle performance and muscle mass in both humans and livestock, including muscle quality in livestock. In this regard, based on the known beneficial qualities of creatine with regard to muscle development and recovery, it is believed that the improvements in solubility and plasma uptake of the creatine HCl of the present invention also lead to significant improvements in muscle development and recovery as compared to creatine monohydrate. Moreover, without being bound to any particular theory, the improvements in the solubility and plasma uptake also reduce or essentially eliminate the negative side effects typically associated with previous forms of creatine.

Creatine HCl Solubility

The creatine HCl of the present invention represents an improvement on prior forms of creatine due to is its remarkably high aqueous solubility. As the low oral absorption of creatine supplements are believed to be attributable at least in part to reduced solubility, the creatine HCl of the present invention is also expected to have better oral absorption properties compared to other forms of creatine.

The creatine HCl of the invention preferably has an aqueous solubility of at least about 150 mg/ml at room temperature. In one embodiment, the creatine HCl preferably possesses an aqueous solubility at room temperature of about 240 mg/mL or greater, more preferably of about 480 mg/mL or greater, and more preferably of about 800 mg/mL or greater. In another embodiment, the aqueous solubility of the creatine HCl of the invention ranges from about 250 mg/ml to about 1000 mg/ml. In yet another embodiment, the creatine HCl has an aqueous solubility of about 400 mg/ml to about 1000 mg/ml. In still another embodiment, the aqueous solubility of the creatine HCl of the invention is at least about 650 mg/ml, preferably at least about 675 mg/ml. For example, the aqueous solubility of the creatine HCl is preferably 679 ± 18 mg/ml when tested at room temperature (25°C) after a time period of about 1.5 hours.

In comparison, the aqueous solubility of other forms of creatine including creatine monohydrate and creatine citrate salt typically ranges from about 10 to about 16 mg/mL.

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