CREATINE

Natural Product

Carl Andersen Tan

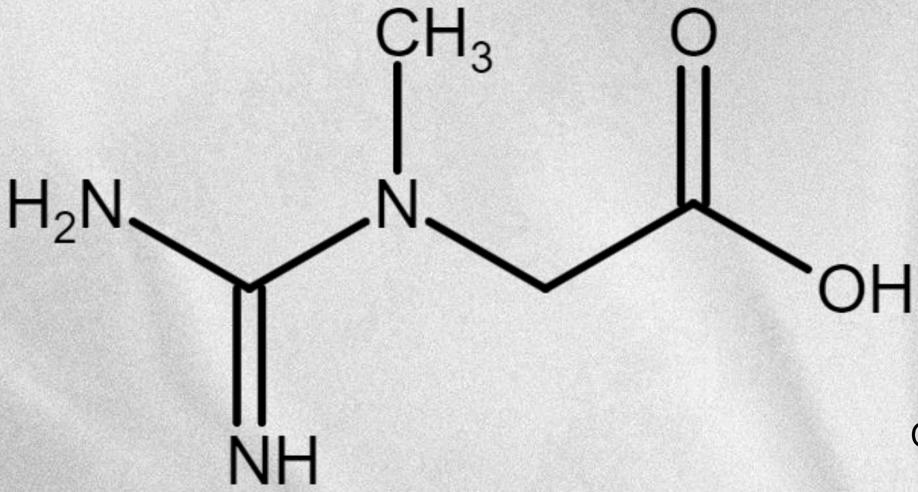
INTRODUCTION

Creatine Supplementation is widely used in sports and gym community to enhance physical performance. Creatine is a small peptide endogenously synthesized in the body and stored in skeletal muscle. Creatine supports the rapid production of adenosine triphosphate (ATP) during high-intensity activities.

TABLE OF CONTENTS

CHEMICAL STRUCTURE

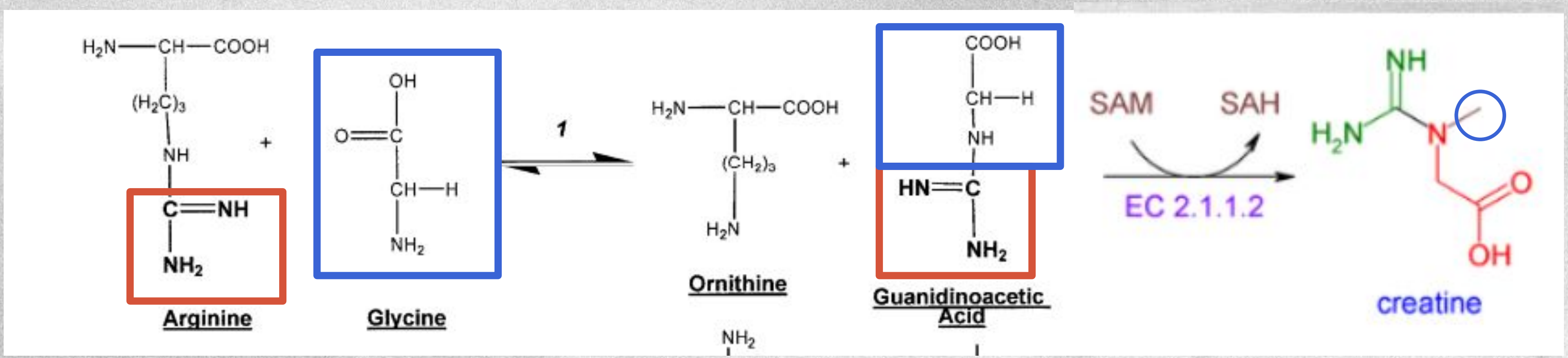
Guanidine group
Composed of two
amino groups (NH_2)
and an imine group
(C(=NH))



Carboxylic Acid Group
(COOH)

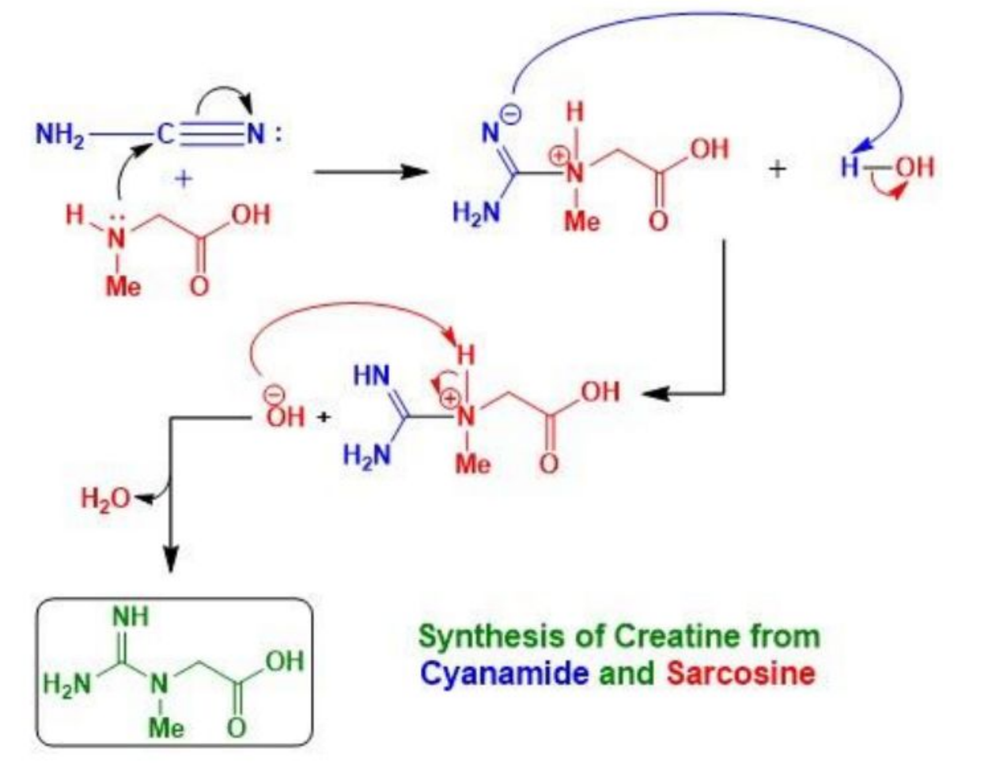
METHYLGUANIDOACETIC ACID

NATURAL SYNTHESIS OF CREATINE



- Creatine synthesis requires three amino acids: arginine, glycine, and methionine.
- First, glycine and arginine form guanidinoacetic acid and ornithine catalyzed by AGAT enzyme.
- Methyl group sourced from methionine in the form of S-adenosylmethionine is transferred to guanidinoacetic acid by GAMT enzyme

INDUSTRIAL SYNTHESIS OF CREATINE



- Industrial Synthesis uses Cyanamide and Sarcosine
- Amine group in sarcosine conducts a nucleophilic attack on nitrile containing carbon group in cyanamide
- Brønsted–Lowry acid–base reaction, Nitrogen atom abstracts a proton from water
- Hydroxyl ion removes a proton from the methyl group

BENEFITS OF CREATINE SUPPLEMENTATION

STRENGTH

ATP Regeneration

MUSCLE HYPERTROPHY

Increases in Insulin like growth factor I

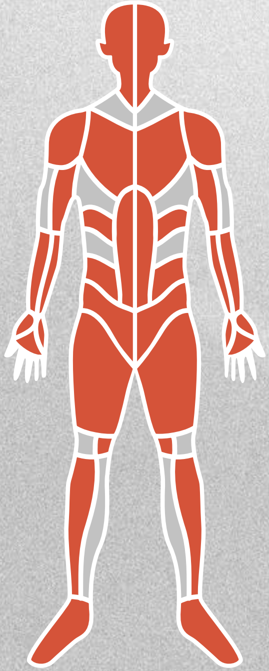
RECOVERY

Activation of mTOR, Antioxidant properties

STRENGTH

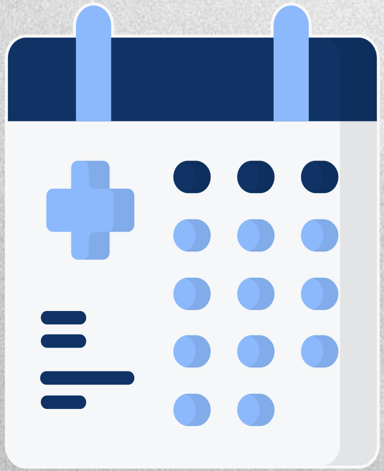
- In the body, creatine is phosphorylated to phosphocreatine through creatine kinase.
- Muscle contraction is an ATP demand heavy process; during exercise, mitochondrial ATP production is not able to keep up with muscle demand causing fatigue.
- When ADP concentrations are high, phosphocreatine is able to donate its high energy phosphate group to regenerate ATP
- Phosphocreatine serves as a method to store energy derived from ATP.

MUSCLE HYPERTROPHY



- Creatine Increases muscle hypertrophy– increase of muscle mass
- Resistance training coupled with creatine supplementation leads dramatic rises in Insulin like growth factor I (IGF-I) concentration within muscles
- IGF-I promotes downstream activation of myogenic regulatory factors (MRFs) such as MyoD and myogenin
- Decreases serum myostatin concentration
- Activation of mTOR pathway. Creatine increases phosphorylation state of 4E-BP1, increasing protein translation.

RECOVERY



- Activates mTOR pathway leading to increased muscle growth and repair
- Creatine exhibits antioxidant properties, research has shown a decrease in 8-OHdG (a marker of oxidative DNA damage) from urine in people supplemented with creatine however exact mechanisms are still unclear.

RESOURCES

Bassit, R. A., Pinheiro, C. H. D. J., Vitzel, K. F., Sproesser, A. J., Silveira, L. R., & Curi, R. (2010). Effect of short-term creatine supplementation on markers of skeletal muscle damage after strenuous contractile activity. European journal of applied physiology, 108, 945-955.

Cooper, R., Naclerio, F., Allgrove, J., & Jimenez, A. (2012). Creatine supplementation with specific view to exercise/sports performance: an update. Journal of the International Society of Sports Nutrition, 9(1), 33.

Deldicque, L., Louis, M., Theisen, D., Nielens, H., Dehoux, M., Thissen, J. P., ... & Francaux, M. (2005). Increased IGF mRNA in human skeletal muscle after creatine supplementation. Med Sci Sports Exerc, 37(5), 731-6.

Kreider, R. B. (2003). Effects of creatine supplementation on performance and training adaptations. Molecular and cellular biochemistry, 244, 89-94.

Louis, M., Van Beneden, R., Dehoux, M., Thissen, J. P., & Francaux, M. (2004). Creatine increases IGF-I and myogenic regulatory factor mRNA in C(2)C(12) cells. FEBS letters, 557(1-3), 243–247. https://doi.org/10.1016/s0014-5793(03)01504-7 .

NIH. (2022). Office of dietary supplements - dietary supplements for exercise and athletic performance. NIH Office of Dietary Supplements. https://ods.od.nih.gov/factsheets/ExerciseAndAthleticPerformance-HealthProfessional/

Persky, A. M., & Brazeau, G. A. (2001). Clinical pharmacology of the dietary supplement creatine monohydrate. Pharmacological reviews, 53(2), 161-176.

Pischel, I., & Gastner, T. (2007). Creatine–its chemical synthesis, chemistry, and legal status. Creatine and creatine kinase in health and disease, 291-307.

Rahimi, R. (2011). Creatine supplementation decreases oxidative DNA damage and lipid peroxidation induced by a single bout of resistance exercise. The Journal of Strength & Conditioning Research, 25(12), 3448-3455.

Saremi, A., Gharakhanloo, R., Sharghi, S., Gharaati, M. R., Larijani, B., & Omidfar, K. (2010). Effects of oral creatine and resistance training on serum myostatin and GASP-1. Molecular and cellular endocrinology, 317(1-2), 25-30.

Study.com (n.d.). synthesis of creatine from cyanamide and sarcosine. Retrieved from https://homework.study.com/explanation/give-a-detailed-mechanism-show-electron-flow-forthe-synthesis-of-creatine-from-cyanamide-and-sarcosine.html

Wyss, M., & Kaddurah-Daouk, R. (2000). Creatine and creatinine metabolism. Physiological reviews, 80(3), 1107-1213.