Reduction of Plasma Creatine Concentrations as an Indicator of Improved Bioavailability

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Background
The retention of dietary creatine is a two-step process; firstly absorption into blood and secondly uptake into the target tissue, principally muscle. Increases in blood plasma creatine concentration are often interpreted as indicating improved bioavailability. However, an increase in the concentration of creatine in plasma could equally be the result of a lower uptake into the target tissue signifying in fact a decrease in overall bioavailability. An increase in circulating insulin in response to glucose administration has previously been shown to increase creatine retention in the muscle. The aim of this study was to compare the effects of ingesting tricreatine citrate (5g, TCrC) with or without the co-administration of 75g of glucose and 200mg of alpha-lipoic acid (TCrC+Glu+ALA, CELL-TECH, Iovate Health Sciences, Oakville, ON, Canada) on creatine concentrations in plasma and urinary creatine elimination during 8 hours following each of the treatments.

Methods
Three male and three female healthy subjects (35.5+/−14.5 yrs, 172.5+/−12.2 cm, 75.3+/−9.0 kg) participated in the study. No subject in this trial was a vegetarian with all subjects reportedly consuming meat in their daily diet. The study used a cross-over design. Each subject received the two treatments, dissolved in 450 ml of water, with 7 days allowed between each treatment. Tricreatine citrate (Creapure™ Citrate, AlzChem, Trostberg, Germany) contains 65% w/w creatine. Results are shown as means together with standard deviation. Primary and derived variables were analyzed by repeated measures ANOVA. Where a significant effect of treatment was indicated, data were further compared using a Bonferroni post-hoc test. The threshold for significance was set at p < 0.05.

Results
Mean peak concentration and AUC were lower in the TCrC+Glu+ALA group in comparison to TCrC (75.3%, p<0.05, and 82.2% respectively). 0.5 and 1h plasma concentrations were significantly lower in the TCrC+Glu+ALA group in comparison to TCrC. Mean urinary creatine elimination over 8 hours was 26.5 ± 13.9% of the dose administered (6.8 ± 3.6 mmol creatine) in the TCrC group, whereas co-administration with glucose and alpha-lipoic acid in the TCrC+Glu+ALA group reduced the mean creatine
elimination to 17.2 ± 13.0% (4.4 ± 3.3 mmol). These results are in keeping with previously published results showing an enhanced rate of creatine uptake into the muscle in the presence of raised insulin.

Figure 1. Mean plasma creatine concentration over 8 hours following ingestion of 5g tricreatine citrate (TCrC) and 5g tricreatine citrate + 75g glucose + 200mg alpha-lipoic acid (TCrC+Glu+ALA)

Conclusion
Lower plasma concentrations measured at 0.5 and 1h and lower peak concentration are consistent with increased rate of uptake of creatine into muscle during this period mediated by an increase in circulating insulin in response to the 75g glucose and 200mg alpha-lipoic acid administered. It appears that the effect is declining after 1h and may require a further administration of glucose. Rather than higher plasma concentrations, lower concentrations in this case are consistent with improved bioavailability. Changes in plasma creatine concentrations, either lower or higher, can only serve as an indication of bioavailability; conclusive evidence can only be obtained from muscle biopsies.

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