

Key Points

- Supplement Creatine through dialysis fluid.
- Improves health, life quality and well-being of dialysis patients.
- Provides a superior treatment by true innovation for dialysis patients and is a unique selling point.
- Offers licensing opportunity with granted patents in USA, Europe, Asia. Patents pending in further regions.

Common Issues for Dialysis Patients

Serious side effects from renal replacement therapy (hemodialysis or peritoneal dialysis) linked to the dramatically reduced Creatine levels in chronic dialysis patients:

- Chronic dialysis patients suffer from dramatically reduced Creatine levels
- Physical and mental fatigue up to depressions
- Neuropathy
- Skeletal muscle weakness and muscle loss
- Neuro-muscular coordination
- Uremic anemia (hypo-proliferative anemia and hemolysis)
- High cardio-vascular co-morbidities
- Anemia related cardio-renal syndrome
- Lowered hypoxia tolerance of the tubular system in the kidney

Creatine is vital for normal body function and cell physiology

The importance of Creatine for normal body function is indicated by established facts:

- Creatine (Cr), is charged-up within the cells to a high-energy compound called Phospho-Creatine (PCr). This energy-rich PCr is then available for regenerating ATP (adenosine-tris-phosphate), the universal energy currency in biological systems, when it is needed for performing cellular work.
- PCr is not only a metabolically inert energy buffer, but also an intra-cellular transport form of energy that is several times more abundant than ATP itself.
- Creatine is one of the most abundant small molecules in the body (the most one after water in muscle).
- Creatine acts as intracellular energy transporter.
- Creatine acts as energy buffer in tissues and cells with high and fluctuating energy demand.
- It is vital for normal brain and nerve function as well as for Heart, skeletal muscle and other tissues and cells of the body, including kidney.
- Cell protection against a number of cell stressors such as hypoxia, free radical (ROS) or toxic stressors etc.

Our solution: Creatine supplementation through dialysis fluid

Creatine added directly to the dialysis fluid! A dialysis process is always a two way process: waste products diffuse from the blood into the dialysis fluid and compounds added to the dialysis fluid diffuse from the fluid into the blood.

- Creatine added to the dialysis fluid, will diffuse back into the patients blood stream and from there will be resorbed by endogenous Creatine transporters and thus reach the target organs and cells in the body to improve their energy state.
- Creatine can be supplied as part of a dialysis kit, making clinical application easy and patient-friendly.
- By using a dry-dialysate cartridge with Creatine, water is added at the bedside of the patient (less transport costs; no formation of Creatinine).



Benefits of Creatine supplementation for dialysis patients

Research indicates that Creatine supplementation increases the overall health, quality of life and well-being of dialysis patients, since Creatine

- Protects blood cells against metabolic and oxidative stress and protects their cell membranes against mechanical stress during dialysis, thus counteracting the loss of red blood cells by hemolysis, leading to anemia (less erythropoietin [EPO] needed).
- Improves muscle cell mass, muscle cell function, proliferation and differentiation and finally overall muscle cell performance (force generation), parameters that are all highly relevant quality of life parameters for hemodialysis patients.
- Lowers fatigue levels, improves memory and learning function, alleviates depressions.
- Enhances bone cell proliferation, differentiation and mineralization thus counteracting, osteoporosis, osteomalacia and adynamic bone disease, problems often encountered in hemodialysis patients.
- Protects body cells and tissues, against oxidative stress, lipid peroxidation, advanced glycation end products.
- Reduces the incidence of hemodialysis associated muscle cramps.
- Infers cardio-vascular protection.
- Supports immune cells and the immune system.

Creatine supply and biosynthesis

- Endogenous Creatine synthesis in the healthy human body supplies only approximately 50% of the total daily Creatine requirement. From the two-step process about 80% of the 1st step occurs in the healthy kidney. The 2nd step of synthesis mainly in the liver: methylation of Guanidinoacetate to Creatine.
- The rest has to be supplied by dietary sources that contain Creatine (meat, fish, milk).
- Creatine occurs only in vertebrates: A 400 g steak contains roughly 2-3 gram of Creatine.
- Ingested Creatine is actively resorbed by a specific Creatine transporter in the intestine. From the blood stream it reaches the target cells and organs that also possess a specific Creatine transporter.

A threefold mechanism leads to the observed dramatically reduced Creatine levels

- Significantly lower endogenous Creatine biosynthesis.
- Washing out of Creatine during dialysis.
- Dietary sources such as fish and meat contain a lot of phosphate and potassium. In fact these patients need a P_i and K^+ - reduced but protein rich diet (1.2g/kg*d body weight protein), for otherwise they frequently get catabolic (protein catabolic rate).

Oral Creatine supplementation is inferior option

- Water intake for patients is restricted (volume control). Combined with the low solubility of Creatine (approx. 12 g/l) it is contra-indicated for the patients to drink the extra water needed for making up a Creatine solution to be ingested.
- High burden of already high pill intake (up to 15/day), and large amount of oral Creatine powder needed (magnitude of 5-10 g/day) further reduces patient compliance and induced additional risk of coughing and choking.

Differentiate: Creatine/Creatinine

- Creatine and Creatinine are not the same!
- Creatinine is the degradation product of Creatine and (Phospho)-Creatine and Creatinine is excreted with urine.
- The Creatinine concentration in the blood is a proxy value (!) for the glomerular filtration rate of the kidney. It is prominent and easy to analyze from blood samples and therefore is generally used in the clinical practice as a marker for renal function. That is, highly elevated serum Creatinine levels are an indication for a general malfunction of the kidneys in that they are no longer able to clear the blood from waste products. However, Creatinine itself is not toxic.

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