

## SUPPLEMENTARY MATERIAL

**TABLE** — Metadata of the articles included in this publication 1-17

Authors	Title	Periodic	Goals	Conclusion
Hespele et al. 2001 <sup>1</sup>	Oral creatine supplementation facilitates the rehabilitation of disuse atrophy and alters the expression of muscle myogenic factors in humans	The Journal of Physiology	To investigate the effect of creatine supplementation during the rehabilitation of an immobilized leg, assessing the recovery of muscle mass and function.	Creatine supplementation significantly accelerates the recovery of muscle mass and strength after a period of immobilization, when combined with rehabilitation training.
Peirano et al. 2011 <sup>2</sup>	Dermal penetration of creatine from a face-care formulation containing creatine, guarana and glycerol is linked to effective antiwrinkle and antisagging efficacy in male subjects	Journal of Cosmetic Dermatology	To assess whether a face formulation containing creatine, guarana, and glycerol penetrates the skin and whether this penetration results in anti-wrinkle and anti-sagging efficacy in men	The formulation has been shown to effectively penetrate the skin and regular use of the product has resulted in a significant improvement in wrinkles and sagging facial skin in men, confirming its effectiveness.
Buford et al., 2007 <sup>3</sup>	International Society of Sports Nutrition position stand: creatine supplementation and exercise	Journal of the International Society of Sports Nutrition	Present the official position of the International Society of Sports Nutrition (ISSN) on the use of creatine supplementation in exercise, critically reviewing the scientific literature on its efficacy, safety and dosage.	Creatine monohydrate is the most effective ergogenic nutritional supplement available to athletes today to increase high-intensity exercise capacity and lean mass. Supplementation, both short-term and long-term, is considered safe and well-tolerated in healthy individuals.
Tyler et al. 2004 <sup>4</sup>	The effect of creatine supplementation on strength recovery after anterior cruciate ligament (ACL) reconstruction: a randomized, placebo-controlled, double-blind trial	American Journal of Sports Medicine	To investigate whether creatine supplementation, combined with rehabilitation, could prevent quadriceps muscle loss or accelerate quadriceps muscle recovery after anterior cruciate ligament (ACL) reconstruction surgery.	Creatine supplementation did not demonstrate any additional benefit in the recovery of quadriceps strength or muscle mass after ACL surgery, compared to the placebo group. The results do not support the use of creatine for this specific purpose.
Candow et al. 2019 <sup>5</sup>	Effectiveness of Creatine Supplementation on Aging Muscle and Bone: Focus on Falls Prevention and Inflammation	Journal of Clinical Medicine	To review the literature on the effects of creatine supplementation on muscle mass, strength, bone health, fall prevention, and inflammation in older populations.	Creatine supplementation, especially when combined with resistance training, is an effective and safe strategy for increasing muscle mass and strength in older adults. These benefits can lead to improved bone health and potentially reduce the risk of falls.
Guo & Dipietro, 2010 <sup>6</sup>	Factors affecting wound healing	Journal of Dental Research	Provide a comprehensive overview of local and systemic factors that can affect the healing process of skin wounds.	Wound healing is a complex process influenced by multiple factors. Local factors such as oxygenation, infection, and the presence of a foreign body, and systemic factors such as age, stress, diabetes, obesity, medications, alcoholism, and smoking can significantly impair the repair process.
Hall et al. 2021 <sup>7</sup>	Creatine supplementation: an update	Current Sports Medicine Reports	Provide an update on the scientific literature on creatine supplementation, addressing its mechanisms of action, effects on performance, potential therapeutic applications, and safety.	Creatine continues to be a highly effective supplement for improving performance in high-intensity exercise, strength and muscle mass. In addition, growing evidence supports its potential use in diverse clinical conditions, such as in neurodegenerative diseases and in the health of the elderly, while maintaining a robust safety profile.
Puthucherry et al., 2013 <sup>8</sup>	Acute skeletal muscle wasting in critical illness	JAMA	To quantify skeletal muscle mass loss and investigate associated cellular changes in patients during the first 10 days of intensive care unit (ICU) stay.	Patients in critical condition suffer a rapid and significant loss of muscle mass right at the beginning of the ICU stay. This loss is associated with changes in protein synthesis and muscle fiber structure, and is more pronounced in patients with multiple organ failure.
Moher et al., 2009 <sup>9</sup>	Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement	PLoS Medicine	Present the PRISMA statement, a set of evidence-based items to improve the quality and transparency of reporting of systematic reviews and meta-analyses.	Present the PRISMA statement, a set of evidence-based items to improve the quality and transparency of reporting of systematic reviews and meta-analyses.
Safdar et al. 2008 <sup>10</sup>	Global and targeted gene expression and protein content in skeletal muscle of young men following short-term creatine monohydrate supplementation	Physiological Genomics	To investigate changes in gene expression and protein content in skeletal muscle in young men after a short period of creatine monohydrate supplementation, without the influence of exercise.	Creatine supplementation, even for a short period and in the absence of training, modulates the activity of a large number of genes. These genetic alterations are involved in important pathways for cell function, muscle growth and osmotic signaling networks, explaining at the molecular level the benefits of creatine.
Santos et al. 2004 <sup>11</sup>	The effect of creatine supplementation upon inflammatory and muscle soreness markers after a 30km race	Life Sciences	investigate the effects of creatine supplementation on markers of inflammation and muscle damage (such as CK, LDH, PGE2, and TNF-alpha) after a 30-kilometer run.	Creatine helped reduce muscle damage and inflammation that typically occurs after exhaustive exercise. The study concluded that supplementation protected the athletes' muscles, resulting in fewer markers of cell injury after the race.
Wyss & Kaddurah-Daouk, 2000 <sup>12</sup>	Creatine and creatinine metabolism	Physiological Reviews	Do a comprehensive review of the literature on how creatine and its byproduct, creatinine, are produced, transported, used, and eliminated by the body.	Creatine is essential for the storage and transport of energy in high-demand tissues, such as muscles and the brain. The article reinforces that while creatine has vital functions and potential therapeutic uses, creatinine (its residue) primarily serves as an important indicator of kidney function.
Antolic et al. 2007 <sup>13</sup>	Creatine monohydrate increases bone mineral density in young Sprague-Dawley rats	Medicine and Science in Sports and Exercise	To investigate whether creatine monohydrate supplementation, with or without exercise (jumping), would affect bone mineral density and bone mechanical properties in young growing rats.	Creatine supplementation resulted in a significant increase in bone mineral density in the rats. This effect occurred in both the exercise and non-exercise mice, suggesting that creatine may benefit bone health directly, and not just as a consequence of increased muscle mass.
Powers et al. 2003 <sup>14</sup>	Creatine Supplementation Increases Total Body Water Without Altering Fluid Distribution	Journal of Athletic Training	Investigate whether creatine supplementation changes the total amount of water in the body and whether it causes a poor distribution of these fluids (i.e., whether it "pulls" water into or out of cells disproportionately).	Creatine supplementation does indeed increase the total amount of water in the body, which is consistent with mass gain. However, the study concluded that this extra water is distributed proportionally between the intracellular and extracellular compartments, giving the lie to the idea that creatine causes cellular dehydration or a harmful water imbalance.
Bender et al., 2008 <sup>15</sup>	Creatine improves health and survival of mice	Neurobiology of Aging	To evaluate the effects of long-term creatine supplementation on the overall health and life expectancy of normal mice.	Lifelong creatine supplementation improved the health of mice, especially in middle age, with benefits on neuromuscular function and protection against neuron degeneration. Remarkably, the mice that received creatine lived, on average, 9 percent longer than the control group.
Finnerty et al. 2013 <sup>16</sup>	The surgically induced stress response	Journal of Parenteral and Enteral Nutrition	Describe the complex physiological, hormonal, and metabolic changes that occur in the body in response to the stress caused by a surgical procedure.	Surgery triggers an intense stress response, activating hormonal and inflammatory systems that put the body in a catabolic state (of degradation). This serves to mobilize energy for healing, but if this response is too intense or prolonged, it can hinder the patient's recovery, increasing the risk of complications.
Kreider et al. 2017 <sup>17</sup>	International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine	Journal of the International Society of Sports Nutrition	Update the International Society of Sports Nutrition's (ISSN) official position on the safety and efficacy of creatine supplementation, incorporating a decade of new research in sport, exercise, and medicine.	Creatine supplementation is not only safe but also beneficial for training performance and health in general, and can be used by people of all ages. In addition to its known effects on sports, there is a growing body of evidence supporting its use to aid in the treatment of various clinical conditions, debunking concerns about its risks.