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Longitudinal monitoring of Cu and Zn isotopes in serum of ICU patients with SARS-Cov-2 infection

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Copper (Cu) and Zinc (Zn) are essential metal trace elements in human body, playing pivotal roles in immune function, metabolic processes, and host defense mechanisms. Owing to its redox-active nature, Cu regulates the production of Reactive Oxygen Species (ROS), thereby contributing to the control of inflammation and oxidative stress (OS) [1-2]. Zinc also exhibits anti-inflammatory and antioxidant properties [1,3] and is a central regulator of immune responses, notably through the modulation of cytokine and chemokine secretion [4]. Severe Covid-19 after infection by SARS-COV-2 is characterized by intense inflammation, cytokine storm, and oxidative stress. Altered serum concentrations of Cu and Zn were also reported in patients' serum with severe disease [1]. In this study, isotopic signatures of Cu and Zn are investigated to evaluate their potential as tracers of disease state and recovery.

A 28-day longitudinal analysis was conducted on Intensive Care Unit (ICU) patients with severe COVID-19 to characterize temporal variations in Cu and Zn isotopic signatures. Because Cu is redox-sensitive, its isotopic composition should be influenced by oxidative stress and redox imbalances. At ICU admission, all patients exhibited enrichment in lighter Cu isotopes. Over the monitoring period, δ^{65}Cu values in most patients progressively increased toward the range observed in healthy subjects, suggesting a gradual restoration of Cu homeostasis as oxidative conditions improved and/or redox balance stabilized.

In contrast, δ^{66}Zn values were characterized by a depletion in lighter Zn isotopes at admission but displayed larger inter-individual variability and no clear temporal trend during follow-up. This behavior may reflect Zn's longer biological turnover time, and the influence of pre-existing factors, which may have already affected the Zn isotopic composition prior infection.

Overall, these findings highlight δ^{65}Cu as a promising biomarker for monitoring disease progression and recovery in severe COVID-19, while emphasizing the greater complexity of interpreting δ^{66}Zn in the context of short-term critical illness.

[1] Engin et al. (2022), *Environmental Toxicology and Pharmacology (95)*, 103937 [2] Rani et al. (2021), *Nutrition Research (92)*, 109-128 [3] Prasad et al. (2009), *Current Opinion in Clinical Nutrition and Metabolic Care (12-6)*, 646-652 [4] Failla et al. (2003), *The journal of Nutrition (133)*, 1443s-1447s