Copper-driven Deselenization: Strategy for Selective Conversion of Copper Ion into Nanozyme and Its possible Implication for Copper-Related Disorders.

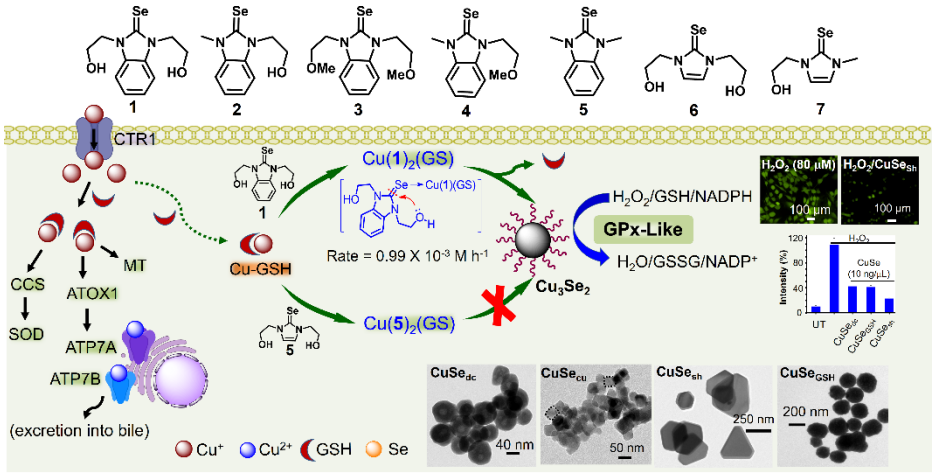
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Abstract: The copper (Cu), an essential trace element to humans, is involved in numerous biological processes in our body. However, the excess Cu is equally detrimental as it produces hydroxyl radical (•OH) from H_2O_2 via Fenton-type reactions, and thereby causes oxidative damage to proteins, lipids, and nucleic acids. The intracellular Cu concentration is, thus, strictly maintained by proteins such as metallothioneines (MTs), ATP7A and ATP7B, ATOX1 and CCS, and endogenous thiol, glutathione (GSH).[1] The majority of cytosolic Cu is bound to GSH, the most abundant intracellular Cu binding ligand of low molecular mass in living cells and is known to be a major contributor to Cu exchangeable pool in the cytosol.[2] Mutation of ATP7B gene results non-functional of ATP7B protein causing Cu over-load in tissues including liver, brain of patients with Wilson's disease (WD) and excess Cu has been implicated in the progression of neurodegenerative disorders including Alzheimer's and Parkinson's diseases.[3] Medical therapy in WD involves lifelong treatment with Cu chelators (penicillamine, trientine) that bind Cu directly in blood and tissues and facilitate its excretion.[4] However, chelation therapy is not always efficient for symptomatic neurological patients and has harmful side effects and,[4] thus, efforts were made to discover tissue specific chelators.[5]

Thus, there is an urgent need to develop new synthetic molecules to cure the copper related disorders. Here, we will discuss the discovery of new synthetic molecule (1,3-bis(2-hydroxyethyl)-1H-benzoimidazole-2-selenone) (**1**)[5] which has remarkable ability to reduce the bioavailability of intracellular Cu concentration by removing Cu from glutathione, a major cytosolic Cu-binding ligand, and thereafter converts it into copper selenide nanozyme that exhibits remarkable glutathione peroxidase (GPx)-like activity with an excellent cytoprotective effect against oxidative stress in hepatocyte.



Citations:

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