

# Copper-ROS-Centered Redox Chemistry in the Brains of Alzheimer's Disease Patients: Biomimetic Type-3 Copper Enzyme Activity and Alternative Redox Insight

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The neurodegeneration in the brains of Alzheimer's disease (AD) patients, often blamed on Reactive Oxygen Species (ROS), is centered around metal-oxygen chemistry. The lack of chemical insight into such systems is a detriment toward understanding the physiology and potential treatment strategies for AD. Herein we present an alternative insight into the copper-oxygen chemistry in AD brains with chemical kinetics and spectroscopic methods. The results indicate the oxidation chemistry carried out by Cu(II)-beta-amyloid(1–20) is consistent with that of the Type-3 copper enzymes polyphenol/catechol oxidase and phenol monooxygenase. The oxidation of catechol oxidation in the presence of the ROS  $\text{H}_2\text{O}_2$  (25 mM) by Cu(II)-beta-amyloid shows  $k_{\text{cat}} = 0.531 \text{ s}^{-1}$  and a significant apparent second-order rate constant  $k_{\text{cat}}/K' = 1,510 \text{ M}^{-1} \text{ s}^{-1}$  from the Hanes plot for a random bi-substrate reaction, wherein the bindings of the two substrates  $\text{H}_2\text{O}_2$  and catechol are independent of each other. It is worth noting that the second-order rate constant for catechol oxidation is only about 20 times lower than that of the catechol oxidase from gypsywort.



