National Institute of Technology Rourkela

Synopsis Seminar

Seminar Title	: Unlocking Ferritin Caged-Iron by Reductive Pathway: Impact of Quinone Redox Cycling with NADH/Ascorbate/O2 and Modified Ascorbates
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Venue	: Seminar Hall, Chemistry Department
Date and Time	: 03 Sep 2025 (4:00 PM)
Abstract	: Ferritin, an iron-storage protein, plays a crucial role in the management of cellular iron homeostasis and prevents iron-induced toxicity. It catalytically sequesters free Fe^{2+} and synthesizes soluble protein-caged ferric-mineral, while ensuring controlled iron-release upon cellular requirements. Given the reducing environment of the cytosol, mainly due to NADH, GSH and AscH, reductive dissolution of ferritin bio-mineral is considered one of the plausible iron release pathway *in vivo*. This work investigates the effectiveness of these reductants in promoting iron mobilization from ferritin, with ascorbate emerging as the most effective, even at lower physiological concentrations, likely due to its small size, pore accessibility, and both one/two electron transfer capability. To further enhance iron-release efficiency, a series of quinones with varying structures and midpoint redox potentials ($E_{1/2}$), were employed as electron mediators separately with ascorbate and NADH.Our findings highlight that reductant-quinone redox couple mediated iron release from ferritin is largely dictated by the molecular structure and $E_{1/2}$ values of quinones along with their reactive oxygen species (ROS) generation properties, *in situ*. Among all quinones, juglone/plumbagin released maximum iron due to their intermediate $E_{1/2}$ values, presence of iron chelation sites and their ability to generate ROS, in situ. Furthermore, ascorbic acid (AA) derivatives (modified at C2/C3/C5-C6 positions) were tested for their stability and redox reactivity. Unsubstituted AA oxidized rapidly at higher pH, while C2/C3-modified derivatives were found to be less reactive. This altered reactivity directly influenced biological function i.e., unsubstituted AA and C5/C6-derivative promoted iron release from ferritin and caused ROS-mediated DNA cleavage, whereas some stable C2 derivatives safeguarded DNA, suggesting safer therapeutic potential. These insights advance our understanding of cellular iron regulation and provide a foundation for developing improved antioxidants, iron-targeted therapies, and antimicrobial strategies.