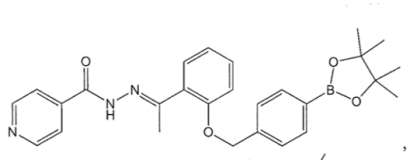
Novel iron chelators that protect cells from oxidative stress

Unmet Need

Metal ions play important roles in the proper functioning of any living organism, but pathologies can develop when metal homeostasis is disturbed. Too much loosely bound iron produces “reactive oxygen species” (ROS) that overwhelm the cells’ antioxidant mechanisms. Many antioxidant therapies rely on molecules that scavenge ROS to mitigate their damage. However, these strategies do not inhibit the formation of ROS. Iron chelation therapy addresses that by inactivating the iron centers themselves. It is effective in cases of systemic metal overloads, such as heavy metal intoxication or iron overload from transfusions. However, in neurodegenerative disorders like Parkinson’s, Alzheimer’s and macular degeneration cellular damage from ROS is caused by metal imbalances that are not systemic but rather localized to a certain organ or subcellular location. Using iron chelators in these cases has serious drawbacks as they unnecessarily decrease iron level in all cells, and their ability to also bind zinc contributes to their toxicity. Advanced design of a “smarter” chelator is needed that would protect cells against ROS damage without causing iron deficiency.

Technology

Duke inventors have synthesized a “masked” chelator that has little affinity for metal ions until the mask is selectively removed by the presence of ROS. In the absence of oxidative stress, these molecules are innocent bystanders incapable of altering metal ion distribution. Disease conditions that elevate oxidative stress, however, activate the chelator to reveal high-affinity iron ligands that compete for loosely bound active iron that is a source of free radicals. This



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Publication(s)

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External Link(s)

• From the lab of Dr. Katherine Franz

chelator demonstrated its ability to protect cells in culture from damage induced by direct addition of hydrogen peroxide as well as by the herbicide paraquat while not altering the iron status in the absence of ROS.

Advantages

- Has been tested on culture cells and shown to efficiently protect hydrogen peroxide and herbicide paraquat
- Has potential for controlled activation by external stimulus
- Has potential to be a neuroprotective drug in treating neurodegenerative deceases