Molybdenum Enzyme Cofactor Research During COVID-19

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Abstract

Molybdenum (Mo) enzymes are ubiquitous in almost every known lifeform. These enzymes exist in simple bacteria, humans, and even date back to the last universal common ancestor. Conservation of the molybdenum enzymes through a billion years of evolution underscores their importance to the health of modern organisms.[1] Molybdenum enzymes have been linked to multiple biological diseases, the nitrogen cycle, and the sulfur cycle. All known molybdenum enzymes possess an identical cofactor (active site), commonly known as the molybdenum cofactor (Moco). The Moco is known to contain a molybdenum metal center, a dithiolene chelate for metal binding, and a pterin appended to a pyran ring known as a pyranopterin. During remote research, the focus of research was to investigate and review various journal articles related to molybdoenzymes, their cofactors, and synthesis projects.

Background

Molybdenum (Mo) is a transition metal that is a trace element found in the Earth's crust or in the oceans, but it is essential to the lives of almost all organisms on Earth, as molybdenum enzymes are used to catalyze many important biochemical reactions, such as respiration in bacteria, detoxification in mammals and avians, and protein synthesis.

Every Mo enzyme possesses a catalytic center involving a single Mo atom bound through a dithiolene ligand to either one or two molecules of a special pyranopterin cofactor. This cofactor was originally called the molybdopterin, but since the cofactor also binds to W, it is better called the metal-binding pyranopterin ene-1, 2-dithiolate (MPT).[2] As all mononuclear molybdenum and tungsten enzymes contain the MPT, the effect of the pyranopterin on the metal center and to the enzyme's function is significant. Since the discovery of the pterin-substituted dithiolene ligand in the MPT, synthetic chemists have been researching the possibility of developing a synthetic replicate.

The Burgmayer Lab has synthesized a similar model system to the biological molybdenum cofactor by binding a pyranopterin to the Mo-coordinated dithiolene ligand. The final synthetic complex is then characterized and studied to gain further insight to the biological Moco.

Literature Research

Current research on molybdoenzymes can be generally divided into 5 categories: investigation of their biological properties, chemical reactivity, electrochemistry, spectroscopy and models.

The articles on biological properties of molybdoenzymes discuss their functions and biosynthetic processes in both prokaryotes and eukaryotes. Many of the articles also focus on the effects of molybdoenzyme deficiencies. Molybdenum enzyme mARC, the fourth mammalian molybdoenzyme, is one of the major focuses of many research, such as its ability to perform reduction of *N*-hydroxylated compounds, its role to activate prodrugs containing amidoxime structures, and its moonlighting properties [3,4,5,6].

Of the articles on chemical reactivity of molybdenum enzymes, the significance of their dithiolene-metal bond and the conformation of the substrate pyranopterin are most often investigated. Many factors can affect the chemical reactivity of molybdenum enzymes during catalysis, and one example is that the conformation and oxidation state of the pyranopterin can modulate the redox potential of the molybdenum center[7].

Electrochemistry of molybdoenzymes is also an area where many studies are being conducted. Redox properties of the metal center and the ligands are of major interests. Many groups have studied Mo-dependent nitrite reduction [8,9]. Other groups have investigated on the effects of changing oxidation states on changes in geometric and chemical structures of Mo-enzymes[10].

Spectroscopic studies, such as electron paramagnetic resonance (EPR) spectroscopy, nuclear magnetic resonance (NMR), infrared spectroscopy (IR), and x-ray crystallography, have been conducted on molybdenum enzymes and their cofactors. Spectroscopic studies are important, because without the context given by the spectroscopic data, results from biological studies sometimes may not be accurate[11].

Also important to the study of any enzymes or cofactors is modeling, which is also one of the focuses of the Burgmayer Group. Various models of molybdoenzymes with Moco have been made, including from the dimethyl sulfoxide family, xanthine oxidase family, and the sulfite oxidase family. There are also research on trying to replace the Mo center in molybdenum cofactors with other metals such as rhenium[12].

Literature Research Continued

Though the research on molybdoenzymes can be generally divided into 5 different categories, more often than not do the articles discuss more than one of the topics, for example, N. Chrysochos et. al.'s article, *Comparison of molybdenum and rhenium oxo bis-pyranzine-dithiolene complexes -- in search of an alternative metal centre for molybdenum cofactor models*, is not only on modeling but also include spectroscopic studies [12]. M. Ahmadi et. al's article, *An Asymmetrically Substituted Aliphatic Bis-Dithiolene Mono-Oxido Molybdenum (IV) Complex With Ester and Alcohol Functions as Structural and Functional Active Site Model of Molybdoenzymes*, also is about modeling and spectroscopies, and they touch upon electrochemistry of molybdenum enzymes[13].

Conclusions

Articles published in scientific journals inform on the current state of metalloorganic synthesis processes around the world. Literature studies provide important background information on the structure and functions of molybdenum cofactors that can be used in future synthetic modeling projects.

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Acknowledgments

We would like to thank Dr. Burgmayer and all the members of the Burgmayer Lab for supporting us. We would also like to thank the Bryn Mawr Summer Science Research Program. Finally, we would like to dedicate this to Emma Allen, graduate student, mentor, and friend.