Thermodynamics of PAH with Iron, Tetrahydrobiopterin, and Phenylalanine

Ashraf Koura*

Department of Chemistry, Mississippi State University, USA

Abstract

This study investigates the thermodynamics of phenylalanine hydroxylase (PAH) interactions with iron, tetrahydrobiopterin (BH4), and phenylalanine. Using Chromobacterium violaceum as a model, we analyze the binding affinities and thermodynamic parameters of PAH in the presence of these ligands. Our findings shed light on the energetics governing PAH activity and provide insights into the molecular mechanisms underlying phenylalanine metabolism.

activity. e presence of iron and BH4 together led to synergistic e ects on PAH activity, suggesting cooperative interactions between these cofactors. e high a nity binding of iron and BH4 to PAH highlights their critical roles in regulating PAH activity and phenylalanine metabolism. e moderate a nity binding of phenylalanine suggests a dynamic regulation of PAH activity in response to changes in phenylalanine concentration. ese ndings provide insights into the molecular mechanisms underlying phenylalanine metabolism and the regulation of PAH activity.

Understanding the thermodynamics of PAH interactions with its ligands may inform the development of therapeutic strategies for phenylketonuria (PKU) and other disorders associated with PAH de ciency. Modulation of PAH activity through targeted interventions aimed at optimizing the availability of cofactors such as iron and BH4 could potentially improve phenylalanine metabolism in patients with PKU [10]. Further studies are warranted to explore the therapeutic potential of manipulating PAH-ligand interactions for the treatment of PAH de ciency disorders. In summary, the results of this study provide valuable insights into the thermodynamics of PAH interactions with iron, BH4, and phenylalanine, shedding light on the molecular mechanisms underlying phenylalanine metabolism and o ering potential avenues for therapeutic intervention in PAH de ciency disorders.

Conclusion

is study investigated the thermodynamics of phenylalanine hydroxylase (PAH) interactions with iron, tetrahydrobiopterin (BH4), and phenylalanine, using Chromobacterium violaceum as a model system. e results demonstrated high-a nity binding of PAH to iron and BH4, highlighting their critical roles as cofactors in regulating PAH activity. Moderate-a nity binding of phenylalanine indicated dynamic regulation of PAH activity in response to changes in substrate concentration.

ese ndings contribute to our understanding of the molecular mechanisms underlying phenylalanine metabolism and the regulation of PAH activity. ey have implications for the development of therapeutic strategies for phenylketonuria (PKU) and other disorders associated with PAH de ciency. Modulation of PAH activity through interventions targeting cofactor availability could potentially improve phenylalanine metabolism and clinical outcomes in patients with PKU. Further research is needed to explore the therapeutic potential of manipulating PAH-ligand interactions and to elucidate the e ects of such interventions on phenylalanine metabolism and neurodevelopmental outcomes in patients with PAH de ciency disorders. Overall, this study provides valuable insights that may inform the development of novel therapeutic approaches for PAH-related disorders.