

Mn(III) and Ga(III) complexes with deferoxamine and its caffeine conjugate as potential antibiotics against marine *Vibrio*

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Highlights

Complexes of Mn and Ga with deferoxamine and its caffeine conjugate present antibiotic activity against two species of marine *Vibrio* causative of coral bleaching.

Abstract

In a scenario of extreme climatic events due to global warming, coral reefs are one of the many threatened ecosystems. With the rise of ocean surface temperatures, beyond thermal and oxidative stress, corals are susceptible to infections from marine bacteria of the *Vibrio* genus, that may cause coral bleaching. Therefore, it is important to seek alternatives that protect corals from such infections. We base our investigations on metal-siderophore complexes as an attempt to apply the bioinorganic strategy known as “Trojan-Horse”.

In this work the conjugate of deferoxamine (DFO) with caffeine, DFCAF, was successfully synthesized and characterized (UV-vis spectroscopy, mass spectrometry, elemental analysis). The complexes Mn^{III}DFO, Ga^{III}DFO and Mn^{III}DFCAF were synthesized and characterized by UV-vis spectroscopy and mass spectrometry. The structure and stability of the complexes were studied through density functional theory (DFT) calculations. Their *in vitro* effects over *V. shilonii* and *V. coralliilyticus* (minimum inhibitory concentration, MIC, and half maximal inhibitory concentration, IC50) were determined and compared with the conventional antibiotic tetracycline (Table 1). Free ligands and metals did not present biological activity. For *V. coralliilyticus*, the MIC of Mn^{III}DFO and Ga^{III}DFO were in the same range as of tetracycline, with Mn^{III}DFO having the closest IC50 value when compared to the conventional antibiotic. For *V. shilonii*, Ga^{III}DFO was notably the best antibiotic tested, with an IC50 value inferior of tetracycline.

It is notable that the observed biological activity is due to the complexed species of M(III) and that the “Trojan-Horse” strategy was successfully applied. Siderophores, which are meant to carry ferric iron into bacterial cytoplasm through specific transport systems, were possibly able to ferry Mn(III) and Ga(III) and produce an antibacterial effect with little likelihood of development of resistance.

Table 1: MIC and IC50 of ligands, metals and complexes against the two species of marine *Vibrio*

Compound	<i>V. shilonii</i>		<i>V. coralliilyticus</i>	
	MIC (μmol·L ⁻¹)	IC50 (μmol·L ⁻¹)	MIC (μmol·L ⁻¹)	IC50 (μmol·L ⁻¹)
DFO	>200	-	>200	-
DFCAF	>200	-	>200	-
Mn ^{III} acetate	>200	-	>200	-
Ga ^{III} nitrate	>200	-	>200	-
Mn ^{III} DFO	25 > MIC > 50	63.66	50 > MIC > 100	47.49
Ga ^{III} DFO	50 > MIC > 100	19.12	50 > MIC > 100	71.01
Mn ^{III} DFCAF	50 > MIC > 100	52.87	>200	109.9
Tetracycline	25 > MIC > 50	30.34	50 > MIC > 100	32.70

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