Metallophores: How do human pathogens withdraw metal ions from the colonized host

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Rok wydania

2023

Wydawca

Elsevier

Miejsce wydania

Amsterdam

Strony

553-574

DOI

10.1016/B978-0-12-823144-9.00086-8

bookChapter.title

Comprehensive Inorganic Chemistry III

ISBN

978-0-12-823153-1

Kolekcja

Naukowa

Język

Angielski

Streszczenie

The increasing interest in metallophores—metal chelating molecules which are excreted outside the pathogen in order to efficiently bind a given metal ion and in their interactions with appropriate metals is one of the results of the dramatic increase of antimicrobial resistance—the resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it. Resistant microorganisms, e.g., bacteria and fungi, are able to withstand the attack of antibiotics and antifungals, making standard treatments ineffective. Novel, effective treatments and ways to specifically deliver them to antibiotic resistant bacteria and to drug resistant invasive mycoses are being actively sought. One of the biggest obstacles in finding such effective, pathogen-specific therapeutics that will not cause severe side-effects in patients arises from the fact that bacteria and fungi share essential metabolic pathways with humans (especially fungi, since they are both eukaryotes). In order to design a highly specific antifungal drug, it is crucial to understand and aim at differences in the metabolism of humans and pathogens. Although pathogen-selective targets are scarce, there is at least one significant difference between the microbial and mammalian cells: the transport system of transition metal ions.

In this chapter, we focus on siderophore and zincophore—based metal transport system, explaining their biological inorganic chemistry, showing metal binding sites, complex geometries and thermodynamic stabilities. Although chemically versatile—siderophores are most commonly small metal chelating agents, while zincophores are more often protein or peptide—based, both classes of metallophores (i) chelate the metal ion in a specific binding mode, (ii) require a binding partner on the pathogen surface, (iii) are a potentially powerful tool for building a Trojan horse strategy based drugs and (iv) are a fascinating phenomenon for bioinorganic chemists.