

## Lanthanide Literature Review: Overview

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### Abstract

**Katherine H. (2016)** It is likely that quite a few of the individuals who read this will be taken aback to realise the extent of the medical applications that may be found for lanthanides. Lanthanides have only recently gained a measure of popularity and more extensive research attention, mostly as a result of the extraordinary success of gadolinium-based MRI contrast agents. This is due to the fact that lanthanides have unique properties that make them useful in a variety of applications. This is partly attributable to the fact that MRI contrast agents based on lanthanides have been in widespread use for several decades. Lanthanides, on the other hand, have a broad variety of additional applications in medicine that are noteworthy. Their usage as hypophosphatemic medications for patients undergoing renal dialysis, as luminous probes in cell research, and for the palliation of bone pain in patients with osteosarcoma are only few examples of the many applications of these compounds. The lanthanides were at one time categorised as rare earth metals; however, it is now known that this classification was incorrect and that they are neither rare nor true earths. The elements that have a position in the 4f orbital are the ones that are referred to as inner transition elements. This definition describes the elements. In general, however, they also consist of La itself and possess the electron shell [Xe]4d16s2. The fact that the ionic radii increase smaller as you advance up the lanthanide series is a characteristic that sets this family of elements apart from others in the periodic table. In most cases, it has been discovered that lanthanide ions are at their most stable in solution when they are in the form of trivalent ions. The only two exceptions to this rule are the element cerium, which can exist as a quadrivalent species, and the element europium, which can also be found as a bivalent species. All of the lanthanides have bioinorganic characteristics that are strikingly similar to those of calcium ion (Ca<sup>2+</sup>). They have roughly the same radii of their ionic constituents, but their charge density is higher overall. Because of this combination, the displacement of calcium in a physiological milieu is an essential issue for a broad range of diagnostic and therapeutic applications. This is because calcium is a cation, which means it can move about in solution.

There were relatively few cases in which lanthanide ions were employed in the treatment of medical diseases prior to the creation of gadolinium-based contrast agents such as Magnevist<sup>TM</sup>. In other words, this was the case before the invention of these contrast agents. Prior to the early part of the twentieth century, there was a gap in our understanding of how to isolate lanthanum and the other lanthanides. This gap prevented us from being able to successfully separate lanthanum. The molecular similarities between the two had, up until that moment, hindered an accurate identification of the substances in question. Lanthanides, in contrast to calcium, frequently display distinct spectroscopic and magnetic signatures. Because of this, lanthanides were an excellent choice for usage as the first medically significant uses of lanthanides. Spectroscopic and magnetic probes were among the first applications of this technology. The vast majority of them give off a brilliant fluorescence when placed in aqueous solutions. In more recent times, a remarkable resemblance between lanthanides and their heavier and sometimes radioactive brothers, the actinides, has been capitalised on to great benefit. This similarity has enabled lanthanides to be used in a variety of applications. Because of this, scientists have been able to identify a number of novel lanthanide compounds. The inclusion of lanthanides into coordination compounds as potential pharmacological agents, both therapeutic and diagnostic, is the most recent innovation that is providing productive results. This is a breakthrough that is producing beneficial results. These chemicals are already shown signs of having potential.

Despite the fact that lanthanides are not always present in biological systems, the danger that can be posed by lanthanides has never been brought into question. As a consequence of this, the vast majority of lanthanum and lanthanide compounds that are utilised in medical contexts are required to possess a high degree of thermodynamic stability. However, lanthanide

carbonate for hyperphosphatemia is a great counter-example that will be explained further on in this study. In most situations, it is better to have quick and entire removal of the lanthanides. **Wehrmann (2019)** reported that *Pseudomonas putida* KT2440, a bacteria residing in the soil, has a significant reliance on its periplasmic oxidation system for its growth on various alcoholic volatiles. The system described herein encompasses the enzyme PedH, which is dependent on the presence of the rare earth element (REE) and pyrroloquinoline quinone (PQQ) for its catalytic activity. The expression of PedH and its Ca<sup>2+</sup>-dependent counterpart PedE exhibits inverse regulation in response to the presence of lanthanides (Ln<sup>3+</sup>), a phenomenon known as the REE-switch mechanism. This study presents empirical findings indicating that the regulation of the REE-switch is impacted by the presence of copper, zinc, and iron. The minimum concentration of Ln<sup>3+</sup> required for the REE-switch to occur is significantly increased by the presence of these elements, regardless of the presence of pyoverdine. The employment of an integrated approach involving genetic and physiological techniques has resulted in the identification of the gene cluster *pedA1A2BC*, which is responsible for encoding an ABC-type transporter system.

This transporter system plays a vital role in facilitating proper growth and development when exposed to low concentrations of Ln<sup>3+</sup> in the nanomolar range. In the absence of *pedA1A2BC*, a much higher concentration of La<sup>3+</sup> is necessary for the growth that relies on PedH, but it does not affect the repression of growth mediated by PedE activity. Based on the data obtained, it can be deduced that the internalisation of lanthanides into the cytoplasm through the *PedA1A2BC* pathway plays a vital role in facilitating the growth of organisms in settings marked by restricted access to rare earth elements (REEs). The results obtained from our research demonstrate that the La<sup>3+</sup> to Fe<sup>3+</sup> ratio exerts an influence on the mechanism responsible for the switching of rare earth elements (REEs). The observed phenomenon can be attributed to the erroneous interaction between potential proteins capable of binding La<sup>3+</sup> ions, such as the histidine kinase PedS2, and an excessive concentration of iron. The present study showcases the complex dynamics of bacterial-metal interactions, highlighting the importance of medium compositions in the investigation of physiological traits in controlled laboratory environments, particularly in the context of phenomena dependent on rare earth elements (REEs).

A research completed by **Paula Roszchenko-Jasińska in 2019** In recent times, the lanthanide elements have been recognised as "novel life metals" in bacterial metabolism. Nevertheless, there are several knowledge gaps pertaining to the mechanisms by which bacteria get, control, and use lanthanides. The formation of formaldehyde is facilitated by the methanol dehydrogenase XoxF, which is dependent on the presence of lanthanides. The accumulation of formaldehyde has the potential to induce fatality in *Methylorubrum extorquens* AM1. The usage of this specific characteristic facilitated a thorough examination of transposon mutagenesis, so contributing to the progress in comprehending the metabolic network that depends on lanthanide elements. The research encompassed the rebuilding of genetically altered strains followed by an examination of their respective patterns of growth. A comprehensive analysis was conducted on over 40 strains, with particular emphasis on clarifying the functions of eight recently identified genes in the context of both lanthanide-dependent and lanthanide-independent methanol development. The genes encompassed in this set comprise a fused ABC-transporter, aminopeptidase, LysR-type transcriptional regulator, putative homospermidine synthase, *mxAD* homolog (*xoxD*), porin family protein, and two genes with unidentified functions that were previously denoted as *orf6* and *orf7* in earlier scientific literature.

The work focused on characterising strains that displayed the lack of particular genes in the lanthanide transport cluster, utilising genetic and biochemical techniques. The aforementioned strains were then assigned the designation "lut," which is an acronym indicating their participation in the utilisation and transportation of lanthanides. The individual genes under investigation have been designated as *META1\_1778* through *META1\_1787*. Consistent with previous research, our study has validated the essential role of the TonB-ABC transport system in facilitating the intracellular movement of lanthanides. Nevertheless, an alternative

mechanism for facilitating the transportation of molecules through the outer membrane became apparent upon prolonging the growth incubations. In addition, the process of identifying suppressor mutations that reinstated the development of the ABC-transporter mutants was conducted. The use of transcriptional reporter fusions has revealed that, akin to iron transport, the expression derived from the promoter of the TonB-dependent receptor lutH is inhibited in the presence of an abundance of lanthanides. Energy dispersive X-ray spectroscopy (EDS) analysis was utilised to examine the spatial distribution of lanthanum in both wild-type and TonB-ABC transport mutant strains. The findings of this study indicate that *M. extorquens* AM1 is capable of storing lanthanides in a mineralized condition inside its cytoplasm.

The assessment of the relevance or value of a certain subject or notion holds paramount importance within the realm of academia. The exploration of the participation of lanthanides in bacterial systems is an emerging field of scholarly inquiry. The present investigation provides insights into the mechanisms by which the methylotrophic bacteria, *M. extorquens* AM1, acquire and sequester lanthanides. The use of lanthanides in modern technology and medical developments is of great importance. However, the extraction of these elements has economic challenges and carries substantial environmental hazards. Methylotrophs have considerable potential as a viable approach for the recovery of lanthanides from diverse sources, including discarded electronic devices, mining leachate, and other forms of waste streams. These microorganisms have exhibited their capacity to perceive and assist the conveyance of these metals, so permitting their application in alcohol oxidation procedures. In addition, methylotrophs have demonstrated high efficacy as biotechnological platforms for the production of diverse chemical compounds. These microbes possess the potential to use pollutants such as methane, as well as inexpensive resources like methanol, rendering them highly valuable for industrial applications. The investigation of the processes behind the acquisition, transportation, and accumulation of lanthanides signifies a notable development in the quest for a sustainable and environmentally conscious method for the retrieval of these elements.

**Samuel James Horsewill's (2021)** examines the current body of research pertaining to lanthanide heterometallic complexes. Additionally, the author presents an innovative approach for the synthesis of lanthanide heterobimetallic compounds. The primary goal of this thesis is to accomplish the previously indicated purpose. The classification of approaches utilised for the regulation of lanthanide heterometallic complex synthesis may be divided into two separate sorts. In syntheses that utilise thermodynamic control, the identification of speciation relies on evaluating the relative binding energies shown by different lanthanides towards specific binding sites of a ligand. The differences in ionic radius and Lewis acidity among the lanthanides result in the development of a predilection for coordination to certain binding sites during equilibrium. In syntheses that utilise kinetic control, the regulation of speciation is governed by the coordination of lanthanide ions to sites with high binding affinity. This coordination leads to the development of a complex that demonstrates kinetic inertness. Following this, the complex experiences alterations to incorporate more metal sites or fragments that contain metal, so reducing the necessity to rely on fluctuations in ionic radius or Lewis acidity. Thermodynamic control has been utilised in the production of heterobimetallic compounds, wherein ligands with selective binding sites for certain sizes are exploited. The utilisation of a solitary ligand, as well as a composite of three functionalized diketonates, has been employed in this methodology.

These diketonates have several binding sites that exhibit preferential affinity towards heterobimetallic and -trimetallic complexes. The preferential binding of lanthanide ions of different sizes was shown in the production of 4-6 triple-stranded helicates with several binding sites. However, subsequent rearrangement of the resultant products was observed. The numerical values under consideration fall within the interval of 7 to 10. In the synthesis of hetero multimetallic compounds under kinetic control, the use of ligands with high affinity is a prevalent strategy for the construction of intricate structures. The covalent coupling of strongly-bound units enables the synthesis of a single ligand that coordinates several lanthanides in an irreversible manner. The initial demonstration of this methodology was

conducted utilising DOTA-type compounds, whereby DOTA denotes 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid. Furthermore, in the field of binding groups, many additional compounds, including cryptates, porphyrins, and phthalocyanines, have been utilised for comparable objectives. Selective demetallation has been utilised in the synthesis of heterobimetallic compounds and in promoting the coordination of lanthanides to reactive pendant groups.

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