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BIOINORGANIC CHEMISTRY OF LANTHANIDES PROBED THROUGH ABSORPTION

Asha Rani

Assistant Professor, Department of Chemistry

Mukand Lal National College, Yamunanagar-135001

ABSTRACT

A puzzling aspect of biological lanthanide use that has important consequences for the translational effect of the biological ligands is why animals investigated up to this time considerably choose early REs even if any RE might be utilized as a competent Lewis acid catalyst. One of the fascinating features of biological lanthanide use is this. This observation, according to our theory, is the outcome of negotiations between several diverse elements. A single group of biological ligands can only retain their singularity within a very narrow range of ionic radius. This is intended to provide the historical context and to hint at that awaits inorganic, physical, and biochemists who choose to explore this line of inquiry. The most attractive features of this field seem to be the opportunity to study biological systems with increasing levels of molecular organization, the wide variety of different physical approaches, and the slow but noticeable changes in chemical properties that occur along the lanthanide series. The environment is rich in the early lanthanides (La, Ce, Pr, and Nd), which are primarily used by biology. They also perform chemistry similar to that of other biologically useful metals, though more effectively due to higher Lewis acidity, and have sufficiently distinct coordination chemistry to permit selective uptake, trafficking, and incorporation into enzymes. There is still a need for additional systematic and thermodynamic research notwithstanding the attempts made to derive certain generalizations.

Keywords: *Bio-Inorganic, Lanthanides, Absorption*

INTRODUCTION

Rare earth elements, which include lanthanides, yttrium, and scandium, are required for the production of a broad variety of modern technologies. These technologies include the permanent magnets used in electric car batteries, wind turbines, and other devices, as well as lasers, phosphors, and imaging agents.[1,2] Rare earth elements are also known as RE elements. However, the insolubilities of REs and other analogous physical characteristics present several challenges for the separation of REs used in applications other than mining or recycling. These challenges pertain to fundamental science, environmental sustainability, and economics. The majority of radioactive elements may be found in phosphate or carbonate minerals, such as bastnasite, monazite, and xenotime. These minerals are considered to be the most abundant sources of REs. Although these lower-grade sources contribute to the challenges of separating REs from more plentiful metal ions, particularly iron, REs may also be found in significant concentrations in coal ash and acid mine drainage.

Rare earth (RE) elements challenges and biological roles of lanthanides

Apart from being used by a few highly specialized enzymes, such as the lanthanide-dependent methanol dehydrogenases found in bacteria, elements and their compounds have no function in living things. The water-soluble compounds are mild to highly hazardous, but the insoluble ones are safe. Due directly to these difficulties a significant amount of investigation has been put into developing novel approaches to differentiate REs from other metals and one another. Some of the methods that are utilized include extremely minute molecules,[5] supramolecular assemblies such as metal-organic frameworks[3], cutting-edge extraction and chromatography technologies, and even bacterial cells[4]. The discovery made in 2011 that some REs (the early lanthanides, La-Nd) are selectively incorporated into PQQ-dependent alcohol dehydrogenases (ADHs) by methylotrophic bacteria has opened up new options for more successful and long-lasting water extraction and separation of these elements. These new possibilities have the potential to make water extraction and separation of these elements more economically viable. These new possibilities have become available as a result of the discovery that some REs,

notably the early lanthanides La-Nd, are selectively digested by methylotrophic bacteria. There has been a discernible rise in the quantity of discoveries made in this region over the course of the preceding year. A significant focus not only on the possible but as of yet unexplained biological activities of lanthanides, but also on the greater ramifications of these results to assist with RE mining, recycling, and separations.

Lanthanoenzymes

The genetic and biochemical characterization of XoxF as a lanthanide- and pyrrole-quinoline quninone (PQQ)-dependent methanol dehydrogenase (Ln-MDH) in several methylotrophs, most notably Methylorubrum (formerly Methylobacterium) extorquens AM1 (Me), demonstrated for the first time in 2011 [6] that lanthanides have a specific biological role. This material was never before disclosed to the general public in any way. Methylotrophs are creatures that acquire all of the carbon that they require from C1 molecules such as methanol or even methane in the case of methanotrophs.[7] Methanotrophs are organisms that get all of their carbon from methanol. For methanotrophs to function, methanol is not required. They may be discovered in the water, the soil, and the plants, all of which are potential players in the carbon cycle due to their presence. MDHs are crucial enzymes for methylotrophs since they catalyze the transformation of methanol into formaldehyde[48]. This transformation takes place in methylotrophic bacteria.

Lanthanide Recognition in Cells

The finding of lanmodulin (LanM) and its subsequent characterization, both of which were reported before the end of 2018,[8] offer the first insights into the biological recognition of lanthanides. Since LanM's amino acid sequence contains four EF-hand motifs, our curiosity about it was piqued almost immediately. EF hands with 12 residues Ca^{II}-binding motifs, widespread in biology and usually found in pairs for cooperative binding, such as in the Ca^{II} calmodulin serves[9] as a sensor. As a demonstration of the parallels in coordination between Ca^{II} and Ln^{III} ions, regular EF hands form bonds with Ln^{III} Having an affinity that is almost one

hundred times higher than Ca^{II}, even though under these circumstances, Ln^{III} coordination has no physiological role.[10]

Lewis acidity, radius, and lanthanide availability compromise

Because members of the lanthanide family have chemical similarities, the Ln-MDH is a useful paradigm for studying metal-dependent structure-function interactions within the context of a single protein framework. This is because of the similarities in the chemistry of the lanthanide family. Mf XoxF (*Methylacidiphilum fumariolicum* solvent V) is capable of growing as a true 'Knallgas' bacteria on hydrogen and carbon dioxide without the input of methane. The whole genome of the SolV strain was analyzed, and it was discovered that there are two genes for hydrogen uptake hydrogenases. These genes encode an oxygen-sensitive enzyme (hup-type) and an oxygen-insensitive enzyme (hhy-type). The molecule that Daumann reported to have the highest degree of activity with Pr.[11] It can be demetalated and reconstituted with all of the lanthanides in vitro and is a versatile chemical. In order to do this, a test based on redox dye was utilized. On the other hand, the results of experiments in which the physiological electron acceptor XoxG was used are distinct from one another. There is no difference in maximum velocity between enzymes with lanthanophore Me La-, Ce-and Nd-XoxFs. On the other hand, the Km for XoxG increases from La to Nd in a manner that is inversely proportional to the ionic radius. These findings provide evidence in favor of our hypothesis that a rise in the Ln^{III}-PQQ cofactor's Lewis acidity leads in an increase in that cofactor's reduction potential (Em). Redox matching between XoxG and the Ln^{III}-PQQ cofactor appears to be a considerable obstacle for the utilization of lanthanides in vivo, as demonstrated by the findings presented here. This idea is given even more weight by the observation that Mf is tolerant of larger lanthanides in vivo, including Gd. Because of this, the Em of Mf XoxG *Methylacidiphilum fumariolicum* SolV) is approximately 80 mV higher than that of Me XoxG. The fact that Me grows with Nd at a slower speed than La does is an additional indication that later REs, it would probably not permit efficient growth. This is because lanthanophore *Me* rises with Nd at a lower rate than La does. The fact that lanthanophore *Me* increases with Nd lends credence to this hypothesis. This leads

one to believe that the lanthanide that is utilized in MDH is a solution that strikes a balance between the radius, availability, Lewis acidity, and Em of its redox partner.[12]

RESEARCH METHOD

Physical Method

The technique of this work is predicated on the hypothesis that the electrical energy levels of lanthanide aquo-ions are very slightly changed when complexes are formed. Under spectroscopy, however, these disruptions, particularly those associated to alterations in the ligand-field symmetry, are usually observable. Dipole-dipole interactions, on the other hand, are particularly notable since they are conveyed via space.[13] These kinds of interactions give rise to a wide range of phenomena, including shifts in resonances of ligand nuclei and increased relaxation rates in those resonances, as well as an increase in the intensity of lanthanide fluorescence. In this aspect, macromolecules, as opposed to extremely minute ligands, give the ability for a lanthanide and a molecule or a molecular fragment to be in close physical proximity to one another without really being linked with one another. Another important distinction is made by the significantly longer molecule tumbling times that are characteristic of macromolecular complexes. This distinction is mostly shown in the nuclear relaxation rates. Because of all of these properties and occurrences, as well as the myriad of ways in which they may be combined, it is possible to apply a wide variety of physical approaches in the exploration of biologically relevant systems by using lanthanides as probes. This is made possible by the fact that lanthanides are relatively abundant. Some of the approaches enable the observation of a property associated with lanthanide ions, while others search for changes in the spectrum of their surroundings.

Optical absorption

The visible and near-ultraviolet sections of the lanthanides' normal crisp but complicated absorption spectra are of relatively modest intensity. The spectral signals demonstrate that the f-orbitals are shielded from the elements of their surroundings in an efficient manner.

Nevertheless, Karraker (1967)[31] revealed that the spectral lines in the region of 500–600 nm associated with the $^4I_{9/2} \rightarrow {}^4G_{5/2}$,$^2G_{7/2}$ Nd^{3+} transitions are sensitive to the formation of complexes and respond accordingly. Haxel, G. B.; Hedrick ((2015) were the first to utilize these "hypersensitive" transitions in order to investigate how lanthanides interact with molecules that are important to biological processes. These authors have shown that distinctive properties may be observed at 520 and 580 nm when a difference spectrum is recorded between two solutions with comparable concentrations of Nd^{3+}, one of which contains bovine serum albumin. This difference spectrum shows that there is a difference between the two solutions. A number of different carboxylic acids, amino acids, trypsin, trypsinogen, and other chemicals were all tested in a series of experiments by the same group of researchers (Lix Z, Zhou L.P , Yan L-L , Dong Y –M , Baiz-L , SunX-Q ,Diwu J ,Warg S, Bunzil J-C, Sun Q-F 2014).[14]

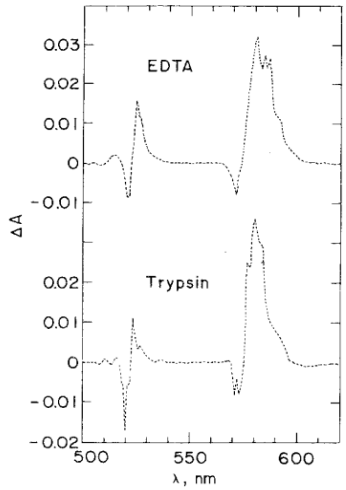

Fig. 1. Absorption spectra of neodymium $^{(III)}$ at pH 5.6 with EDTA and trypsin. reconstruction based on Darnall et al. Concentrations: EDTA 87.5 mM, Nd $^{3+}$ 26 mM, trypsin 0.37 mM, Nd $^{3+}$ 3.74 mM.

X-ray crystallography

When doing X-ray crystallographic research on macromolecules, each of the lanthanides produces anomalous scattering components of X-ray light. These components have the potential to assist in the phase determination process. According to Cromer's research from 1965, Sm $^{3+}$, Nd $^{3+}$, and Eu $^{3+}$ all exhibit extremely substantial dispersion. In most cases, the protein or nucleic acid crystals first need to be synthesized, and then they must be suspended in a solution of lanthanide salt. After diffusing inside the crystal, the cations will presumably bond to the sites with the highest attraction after they have already done so. Some of these macromolecules include proteins, lipids, and nucleic acids. Gao H.Y., Peng W.L., Meng P.P , Feng X.F. (2014) are the only researchers that have characterized the lanthanide binding site in thermolysin and lysozyme, respectively.[15]

Bioinorganic chemistry

The same well-established laws of lanthanide coordination chemistry regulate the interactions of lanthanide ions with molecules of biological importance. These rules govern the interactions of lanthanide ions with molecules of biological relevance. According to these principles, the interactions are predominately electrostatic, the bonds that form have a high degree of ionicity, charged oxygen donors are favoured as ligands, and dehydration of the aquo-ion has a substantial impact on the thermodynamics of complex formation. Differences in some of these characteristics may be seen across the lanthanide series. These differences are all tied to the ionic radius contraction. It's possible that this will become clear after the lanthanide series is developed. There is always the possibility that something called a "gadolinium break" or another type of subgroup split will take place. By highlighting the parallels that exist between Ca^{2+} and lanthanides, one is able to either defend or encourage the process of isomorphous replacement in biological macromolecules. The coordination numbers, ligand exchange rates, and ionic radii are among of the aspects in which these parallels are most apparent. Using ultrasonic relaxation methods, Bonificio W.S. , Clarke D.R. (2014) evaluated the likelihoods of Er^{3+} and Ca^{2+} to form inner-sphere lanthanide complexes with the perchlorate ion in environments with varying dielectric constants. These environments contained Er^{3+} and Ca^{2+} lanthanide ions. He came to the conclusion that Er^{3+} was a more likely candidate to generate these complexes than Ca^{2+}. The likelihood of $Er^{3+}$and Ca^{2+} to form these complexes in media with varying dielectric constants was analyzed, and the results led to this discovery.[16]

DATA ANALYSIS

Amino acids, peptides, and related derivatives

Amino acids serve as the fundamental building blocks for the structure of proteins. Aqueous solutions with a pH in the range of 3–8 are where they are found as the amphiionic radical with the notation $^{+}NH_3CH(X)COO^{-}$. In the purpose of this discussion, the amino acid side chain is referred to as group X. At the site of the ionized carboxyl group is where it is hoped that the link with lanthanides will take place. On the other hand, due to the near proximity of the positively charged amino group, it is anticipated that the formation of complexes will be less robust than it

would be with simple carboxylates. This can be explained by the fact that simple carboxylates do not have such a close proximity. An outstanding demonstration of this activity is provided by Park D.M.,Brewer A, Reed D.W., Lammers L.N., Jiao Y (2014) in the form of the Dy^{3+}-induced proton alterations in the sequence of glycine and its related peptides. In these kinds of circumstances, the shift gradually distancings the positively charged group from the carboxyl terminus that is complexing causes the group to migrate farther away. The dissociation constants for Eu^{3+} complexes are reported to be 0.08 M for glycine and $3.2\ 10^{-3}$ M for triglycine, as stated by Nieboer et al. (2014). On the other hand, the dissociation constant of the monoacetato complex is calculated to be $4.9\ 10^{-3}$ M(Molarity), as stated by Kolat and Powell (2013). In view of the pH sensitivity of Nd^{3+}-induced alterations, Sherry and her colleagues (2015) proposed a proposal about bidentate coordination with histidine. This idea included the involvement of a ring nitrogen as a participant.[17]

Studies on the formation of complexes involving lanthanides and carboxylic acids frequently make use of potentiometry as an analytical tool. Hibi Y, Asai K , Arafuke H, Hamajime M, Iwama T, Kawai K (2015) have only recently completed extensive potentiometric and circular dichroism investigations with amino acids. They came to the conclusion that the primary effects that were observed were the result of the hydrolysis of lanthanide ions in neutral solutions, and that these findings could not be utilized to make any inferences regarding the amino acid complexes of lanthanides. This was the conclusion that they came to after doing their research. In order to observe, via the use of potentiometry, the formation of complexes with amino acids, measurements have to begin with the cationic form of amino acids that may be detected in acidified solutions. These kinds of investigations were carried out in 2014 by Sherry and her colleagues, and the results are in good accordance with the NMR data.[18]

Table 1. Dissociation constants of 1 : 1 lanthanide-amino acid complexes

	Amino acid	KD (M)	pH	Temp. (°C)Method	
La	Sarcosine	0.25	3-8	25	NMR
Nd	Alaninc	0.23	-	22	Potent.
Nd	Alanine	0.15	4.0	22	NMR
Nd	Histidine	0.50	4.0	22	NMR
Nd	Serine	0.10	-	22	potent.
Nd	Serine	0.08	4.0	22	NMR
Nd	Threonine	0.13	4.0	22	NMR
Pr	Alanine	0.30	4.6-5.0	39	NMR
Pr	Ampicillin	0.13	4.0-4.6	25	NMR
Eu	Glycine	0.20	3.6	25	partition
Eu	Glycine	0.08	3.8	-	NMR
Eu	Alanine	0.18	3.6-4.5	25	partition
Eu	Azetidine-2-earboxylate	0.28	4.6-5.0	37	NMR
Lu	Sarcosine	0.13	3-8	125	NMR

Fitriyanto N.A. , Fusimi M ,(2014) investigated the molecular conformation of a variety of penicillins, hydroxy-L-proline, and a large number of cyclic amino acids in solution by utilizing lanthanide-induced shifts and line-broadenings. Lanthanide-induced shifts have a number of applications, including the assignment of peptide spectrum characteristics and the identification of individual sequences.[19]

High frequency NMR spectrometers, such as those operating at 300 MHz, give improved resolution and bigger shifts, allowing for the study of hexa- or even heptapeptides. This makes it possible to study longer peptide chains. According to Nakagawa T , MitsuR , Tani A, (2014) the variations in the carbon-13 spectra ought to be useful in this regard as well.[20]

Using nuclear magnetic resonance in conjunction with potentiometric titrations Martinez – Gomez NC , VU H.N., Skovran E., (2015) [21] studied the interactions that occur between N-acetyl-L-3-nitrotyrosine ethyl ester and the lanthanides. This molecule's ionized ortho-nitrophenolate moiety, which has a pK value of 7.09, chelates R^{3+} ions. The pK value refers to the acidity of the molecule. The constants of dissociation for the chelates of La^{3+}, Eu^{3+}, Pr^{3+}, and Gd^{3+}, respectively, are 5.1, 2.2, 2.5, and 3.1 mM. In-depth study within the context of a non-axial model to investigate the proton shifts and line-broadenings that are brought on by

lanthanides. As a consequence of their discovery, it is possible that the information contained in proteins containing nitrotyrosyl groups, which have the potential to operate as a particular lanthanide binding site, will be better understood. The reaction that produces Schiff bases involves pyridoxal and amino acids interacting with one another. Bogart J.A., Lewis A.J. , Schelter E.J. DFT (2014), [22] conducted research on the luminescence of the latter NMR lanthanide-amino acid complexes and presented this notion as a way for determining the residue that is positioned at the N-terminus of peptides and proteins.

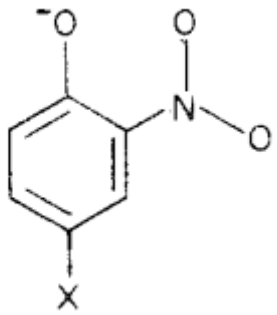

Figure 2 Amino acid lanthanides series ionized carboxyl group

Carbohydrates

Because of Prejano M, Marino T, Russo N., (2015)[23] metal ion-sugar complexes are experiencing a resurgence in their level of appeal. In the beginning, Angyal utilized lanthanide ions for the purpose of acting as shift reagents for carbohydrates in aqueous solution. Polyols and carbohydrates in general will bind metal ions if they contain three cis hydroxyl groups on adjacent carbon atoms that can generate an ax-eq-ax configuration. Lanthanide ions sequence of metal ions has the most potential to form complexes with D-allose. Na^{+}, y^{3+}, Ca^{2+}, and La^{+}. Polyols and carbohydrates in general will bind metal ions if they have these characteristics. Lenkinski and Reuben (2014) discussed the methods for interpreting proton NMR data in systems where metal ion-sugar complexation occurs. They also dealt with the data collected for the interaction of Ca^{2+} and La^{3+} with D-lyxose and D-ribose. Lumpe H , Pol A , OP den camp H.J.M , Daumann L.J.(2013) also dealt with the data acquired for the interaction of Ca^{2+} and La^{3+} with D-ribose. The information acquired on the interactions between Ca^{2+} and La^{3+} and

D-lyxose and D-ribose can be analyzed with these approaches if necessary. The conclusions of their investigation that if one of the coordinating hydroxyl groups were to be converted into a methoxy group, the relationship would not be severed. In 1975a, Cotton S.A. , Raitby P.R. (2016) made the seminal discovery that it is possible for Eu^{3+} and methyl-**α** -D-gulopyranoside to create a 1:1 complex. This discovery was a game-changer in the field.[24,25]

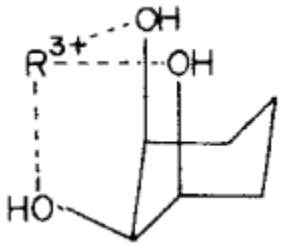

Figure 3 Lanthanide chelation

Studies using nuclear magnetic resonance (NMR) have shown that lanthanides are amenable to being chelated by the anions of D-galacturonic acid and its derivatives. According to Shannon R.D. (2014) complexes with a 3:1 ratio tend to emerge in this particular environment. The presence of Gd^{3+} generates stereospecific relaxation effects in the uronic acid proton and carbon-13 spectra. It may be deduced from this that this can be utilized as a diagnostic tool for the purpose of differentiating between various anomeric forms. When Seitz M, Oiver A.G. (2014) investigated the effect that Gd^{3+} has on the proton relaxation rates of a variety of mono- and di-saccharide sugars, they discovered findings that were comparable to one another.[26, 27]

Table 2. Ca^{2+} and La^{3+} complexes with sugars' dissociation constants (at 52 °C)

Sugar	K_D^{Ca}(M)	K_D^{La}(M)
β -D-lyxopyranose	1.25 ± 0.15	1.0 ± 0.1
α-D-ribofuranose	0.45 ± 0.05	0.18 + 0.01
α- D-ribopyranose	0.71 ±0.05	0.28±0.01
β - D-ribopyranose	1.45 ±0.2	1.1 ±0.t

Nucleotides

In a wide number of enzyme processes, nucleotides play the role of either substrates or cofactors. Typically, nucleotides are found in the form of their metal ion complexes. They can also be thought of as the monomers that make up DNA and RNA. R.J.P. Williams and his colleagues at Oxford have conducted substantial research on the topic of lanthanide complexes of nucleotides. Regarding these complexes, there are two important points to take into consideration. The structure of a nucleotide in solution may be determined with the help of NMR by employing techniques such as line-broadenings and lanthanide-induced chemical shifts. According to Tanswell et al.'s research from 1974, lanthanide nucleotide complexes have several applications in enzymatic operations. These applications include acting as competitive inhibitors, paramagnetic probes, and mapping enzyme binding sites.

NMR research has shown that compound formation between lanthanides and nucleotides occurs at a pH level of roughly 2, which is considered to be quite low. The dissociation constants are shown in the table in a condensed form. Horrocks W.D. , Sudnick D.R. (2013) demonstrated that the phosphate group present in nucleotide monophosphates functions as a bidentate ligand. Within the ATP Complex, the lanthanide ion communicates with the terminal phosphates, each of which most likely performs the function of a tetradentate ligand. In addition, research have shown that complex formation can occur with sugar phosphates. At higher pH levels, the R(EDTA)- chelates bind with both mono- and di-nucleotides. This is something to keep in mind since it could be intriguing. In the complexes with glucose-6-phosphate, the dissociation constants were at about 15 mM.[28]

Table 3 Dissociation constants of lanthanide complexes including xylitol (at 39 °C)

R^{3+}	K1(M)	K2(M)
Pr	0.5 ±0.1	8 ±4
Nd	0.25±0.01	2.0±0.1
Eu	0.26±0.04	1.3±0.3

When the nucleotides reach pH levels that are higher than neutral, they completely ionize, and the formation of complexes with lanthanides is more beneficial. As a consequence of this, fluorescence experiments gave Formoso (2014) the ability to estimate a dissociation constant for Tb^{3+} complexes of nucleotide monophosphates that was the order of 1 mM even when the pH was 5.6. Using a competitive spectrophotometric technique, Ellis and Morrison (2013) determined that the equilibrium concentration of the Eu^{3+}-ADP combination at pH 7 was 10^{-6}M. Gadolinium able to displace the Mn^{2+} that is present in the Mn^{2+}-ATP combination. By measuring the amount of free Mn^{2+} using EPR, were able to determine that the Gd^{3+}-ATP combination has a dissociation constant of 10^{-7}M when it is at a pH of 6.0., higher pH levels result in a stronger binding, which leads to slower ligand exchange rates.

Lanthanides have been shown to be useful in providing spectrum resolution for nuclear magnetic resonance (NMR) examinations of cyclic nucleotides . The magnitudes of lanthanide-induced chemical shifts and line-broadenings have been investigated in terms of molecular structure in research including mononucleotides, cyclic nucleotides, dinucleotide phosphates, ATP, and cyclic nucleotides It is interesting to note that MulQueen P, Tingey J.M. , Horrocks W.D.J ,(2014). demonstrated that the conformation of AMP in dimethylsulfoxide (DMSO), as measured by physical spectroscopic method, was different from the conformation of AMP in water .[29]

Proteins and enzymes

The interaction of lanthanides with proteins is one of the subfields of lanthanide bioinorganic chemistry that has garnered the most interest from researchers. In this part of the article, we will provide an overview of the interaction that occurs between lanthanides and proteins, including

how this connection influences the activity of enzymes. After that, a more in-depth discussion is held about the discoveries that were achieved by using some of the systems.

Modifications to the protein spectrum, modifications to the lanthanide spectrum, and modifications to the proton relaxation times of the water of hydration are the three broad categories that best describe the spectral perturbations that can result from the formation of a complex between a lanthanide ion and a protein. There is a possibility that the binding to a few additional proteins can be deduced from X-ray pictures and enzymatic activity, but testing has not yet been done, and doing so at this time would either be impractical or impossible. While the La^{3+}-porcine trypsin complex was found to have a dissociation constant of $5.6_X\ 10^{-3}$ M (log K_A = 2.26), the Eu^{3+}-inorganic pyrophosphatase complex was found to have a dissociation constant of 2.3 10^{-7} M (log K_A "- 6.64). The utilization of a wide range of lanthanide protein complexes allowed for the acquisition of these findings. It is difficult to coherently explain either this range as a whole or any individual figure when further information is not available.

It would be very helpful to get thermodynamic data and constants for a greater number of different lanthanides that were complexed with the same protein. Epstein et al. published their findings on porcine trypsin in 1974 and 1977, which is largely responsible for its widespread dissemination. The variation in log K_A that takes place when the lanthanide ionic radius is altered in porcine trypsin and nitrilotriacetate (NTA) complexes. This variation takes place when the lanthanide ionic radius is altered. The two distinct collections of data are astonishingly identical to one another, despite the fact that the absolute values of the constants differ by eight or nine orders of magnitude. This parallelism lends credence to the spectroscopic findings published by Bentrop D , Bertini I , Cremonini M.A. , Forsen S , Luchinat C, malmendal A (2012), which demonstrate that the ionized carboxyl groups found in proteins are coordinated to lanthanides. The synthesis of lanthanide complexes is often an entropy-driven process. The process of chelation results in significant alterations to entropy. The changes in enthalpy vary from 0.4 to 2.6 kcal/mole, and they are not only insignificant but even positive. This is due to the fact that changes of 52.2-63.8 e.u., which are equivalent to

15.6-19.0 kcal/mole at 25^{O}C, follow chelation by NTA. Variations in the stability constants of NTA chelates along the lanthanide series may be traced back to the primary cause, which is the different entropies that can be seen across the lanthanide series. When compared to the findings obtained with porcine trypsin, these results make it abundantly clear that this might also be the case with protein complexes.[30]

$$\ln K_A = -\Delta H^0/RT + \Delta S^0/R \quad \text{.....(Eq.1)}$$

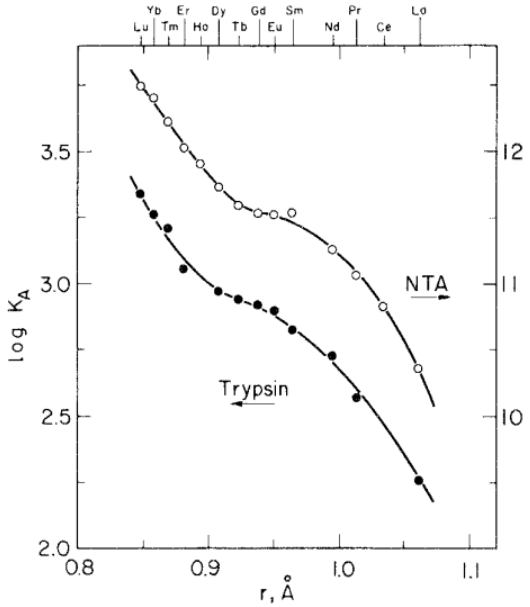

Fig. 4. The dissociation constants of Gd^{3+} complexes with bovine serum albumin (BSA, Filled circles) and porcine trypsin (open circles) as a function of temperature.

There is a temperature-dependent change in the dissociation constants of the Gd^{3+} complexes formed with porcine trypsin and bovine serum albumin (BSA). The constants of dissociation demonstrate that the creation of complexes is an endothermic process, and this remains true even as the temperature increases. It has been demonstrated that endothermic bonding may take place between glycine and Ce, Pm, and Eu^{3+}, as well as between lysozyme and Gd^{3+} 3+.Based on the examination of the data for BSA and trypsin, it is clear that entropy plays a driving role in the binding process. An overview of the thermodynamic properties of NTA and EDTA chelates along with specific information on those chelates. The fact that microchelates have

significantly higher positive enthalpies than macromolecular complexes is the primary characteristic that sets them apart from one another. When complexes are formed, there is often a significant loss of water, which is commonly thought to be the cause of entropy fluctuations that take place throughout this process. The hydration entropy of Gd^{3+} is 98 equivalent units. Assuming that the entropies of complexation with proteins are entirely caused by dehydration, the results imply that the Gd^{3+} ion has lost more than 35% of its water of hydration after complexation with BSA and more than 70% after complexation with trypsin. This is the case because the data suggest that the Gd^{3+} ion has lost more than 70% of its water of hydration. Due to the fact that the hydration number of the aquo-ion is 8, there can only be 5.2 or 2.4 water molecules in the coordination sphere when a Gd^{3+} ion is connected to BSA or trypsin, respectively. This is because the aquo-ion has a hydration number of 8 in its structure.

CONCLUSION

As of the beginning of 1976, the present state of lanthanide bioinorganic chemistry as well as the use of lanthanides as probes to investigate physiologically intriguing systems were being studied. This article's purpose is to provide background knowledge while also offering a glimpse of the excitement that is in store for inorganic, physical, and biochemists who decide to follow this field of research. The modest but perceptible variations in chemical features along the lanthanide series, the vast range of physical techniques, and the possibility to explore biological systems with increasing degrees of molecular structure appear to be the most appealing components of this field of study. Even though some generalizations have been attempted to be derived, there is still a requirement for more systematic and thermodynamic study. The results of their research will undoubtedly lead to an expansion of our knowledge of the chemistry of lanthanides in general, as well as bioinorganic chemistry.

REFERENCES

[1] Haxel G B. Hedrick J B. Orris G J. Rare earth elements - Critical resources for high technology. U.S.G.S. Fact Sheet 2002; 087– 02. DOI: 10.3133/fs08702

[2] Kostelnik T I. Orvig C. Radioactive main group and rare earth metals for imaging and therapy. Chem. Rev. 2019; 119: 902– 956. DOI: 10.1021/acs.chemrev.8b00294

[3] Firsching F H. Brune S N. Solubility products of the trivalent rare-earth phosphates. J. Chem. Eng. Data 1991; 36: 93– 95. DOI: 10.1021/je00001a028

[4] Evans C H. Biochemistry of the Lanthanides. Plenum Press: New York, 1990.

[5] Yang X J. lin A. Lix L. Zhou W. Chen Z. China's ion-adsorption rare earth resources, mining consequences and preservation. Environ. Dev. 2013; 8: 131– 136. DOI: 10.1016/j.envdev.2013.03.006

[6] Arshi P S. Vahidi E. Zhao F. Behind the scenes of clean energy: The environmental footprint of rare earth products. ACS Sustainable Chem. Eng. 2018; 6: 3311– 3320. DOI: 10.1021/acssuschemeng.7b03484

[7] Bomgardner M M. The struggle to mine rare earths. Chem. Eng. News. 2015; 93 (30): 36– 39.

[8] Chession T. Schelter E J. Rare earth elements: Mendeleev's bane, modern marvels. Science 2019; 363: 489– 493. DOI: 10.1126/science.aau7628

[9] Long K R. Vangosen B S. Foley N K. The Principal Rare Earth Elements Deposits of the United States: A Summary of Domestic Deposits and a Global Perspective. In Non-Renewable Resource Issues. International Year of Planet Earth; Sinding-Larsen, R., Wellmer, F. W., Eds.; Springer: Dordrecht. 2012.

[10] Xie F. Zhang T A. Dreisinger D. Doyle F A. Critical review on solvent extraction of rare earths from aqueous solutions. Miner. Eng. 2014; 56: 10– 28. DOI: 10.1016/j.mineng.2013.10.021

[11] Erickson B. Rare-earth recovery: U.S. efforts to extract valuable elements from coal waste surge. Chem. Eng. News 2018: 96 (28): 29– 33.

[12] Bogart J A. Cole B E. Boreen M A. Lippincott C A. Manor B C. Carroll P J. Schelter E J. Accomplishing simple, solubility-based separations of rare earth elements with complexes bearing size-sensitive molecular apertures. Proc. Natl. Acad. Sci. U. S. A. 2016: 113: 14887– 14892. DOI: 10.1073/pnas.1612628113

[13] Fang H. Cole B E. Qiao Y. Bogard J A. Chession T. Menor B C. Caroll P J. Schelter E J. Electro-kinetic separation of rare earth elements using a redox-active ligand. Angew. Chem. ,Int .Ed. 2017; 56: 13450– 13454. DOI: 10.1002/anie.201706894

[14] Lix Z. Zhou L P. Yan L L. Dong Y M. Baiz L. Sun X Q. Diwu J. Warg S. Bunzil J C. Sun Q F. Supramolecular lanthanide separation approach based on multivalent cooperative enhancement of metal ion selectivity. *Nat. Commun.* 2018; *9*: 547. DOI: 10.1038/s41467-018-02940-7

[15] Gao H Y. Peng W L. Meng P P. Feng X F. Li J Q. Wuh Q. Yan C S. Xiong Y L. Luo F. Lanthanide separation using size-selective crystallization of Ln-MOFs. Chem. Commun. 2017; 53: 5737– 5739. DOI: 10.1039/C7CC01898C

[16] Bonificio W S. Clarke D R R. Rare-earth separation using bacteria. Environ. Sci. Technol. Lett. 2016; 3: 180– 184, DOI: 10.1021/acs.estlett.6b00064

[17] Park D M. Brewer A. Reed D W. Lammers L N. Jiao Y. Recovery of rare earth elements from low-grade feedstock leachates using engineered bacteria. Environ.Sci.Technol. 2017; 51: 1347113480, DOI:10.1021/acs.est.7b02414.

[18] Hibi Y, Asai K. Arafuke H. Hamajime M. Iwama T. Kawai K. Molecular structure of La^{3+}-induced methanol dehydrogenase-like protein in Methylobacterium radiotolerans. JBiosci.Bioeng. 2011; 111: 547– 549, DOI:10.1016/j.jbiosc.2010.12.017

[19] Fitriyanto N A. Fusimi M. Matsunaga M. Pertiwingrum A. Iwama T. Kawai K. Molecular structure and gene analysis of Ce^{3+}-induced methanol dehydrogenise of Bradyrhizobium sp. MAFF211645. J. Biosci. Bioeng. 2011; 111: 613– 617, DOI: 10.1016/j.jbiosc.2011.01.015

[20] Nakagawa T. Mitsu R. Tani A. Sasa K. Tashiro S. Iwama T. Hayakawa T. Kawai L. A catalytic role of XoxF1 as La^{3+}-dependent methanol dehydrogenase in Methylobacterium extorquens strain AM1. PLoS One. 2012; 7e50480. DOI: 10.1371/journal.pone.0050480

[21] Martinez – Gomez N C. Vu H N. Skovran E. Lanthanide chemistry: From coordination in chemical complexes shaping our technology to coordination in enzymes shaping bacterial metabolism. Inorg. Chem. 2016; 55: 10083– 10089, DOI: 10.1021/acs.inorgchem.6b00919

[22] Bogart J A. Lewis A J. Schelter E J D F T. Study of the active site of the XoxF-type natural, cerium-dependent methanol dehydrogenase enzyme. Chem. - Eur. J. 2015; 21: 1743– 1748. DOI: 10.1002/chem.201405159

[23] Prejano M. Marino T. Russo N. How can methanol dehydrogenase from Methylacidiphilum fumariolicum work with the alien Ce^{III} ion in the active center? A theoretical study. Chem. - Eur. J. 2017; 23: 8652– 8657. DOI: 10.1002/chem.201700381

[24] Lumpe H. Pol A O P. Den-camp H J M. Daumann L J. Impact of the lanthanide contraction on the activity of a lanthanide-dependent methanol dehydrogenase - a kinetic and DFT study. Dalton Trans. 2018; 47: 10463– 10472. DOI: 10.1039/C8DT01238E

[25] Cotton S A. Raitby P R. Systematics and surprises in lanthanide coordination chemistry. Coord. Chem. Rev. 2017; 340: 220– 231. DOI: 10.1016/j.ccr.2017.01.011

[26] Shannon R D. Revised effective ionic radii and systematic studies of inter atomic distances in halides and chalcogenides. Acta Crystallogr., Sect. A: Cryst. Phys., Differ., Theory. Gen. Crystallography. 1976; 32: 751– 767. DOI:10.1107/S0567739476001551

[27] Seitz M. Oiver A G. Raymond K N. The lanthanide contraction revisited. J. Am. Chem. Soc. 2007; 129: 11153– 11160, DOI: 10.1021/ja072750f

[28] Horrocks W D. Sudnick D R. Lanthanide ion probes of structure in biology. Laser-induced luminescence decay constants provide a direct measure of the number of metal-coordinated water molecules. J. Am. Chem. Soc. 1979, 101: 334– 340. DOI: 10.1021/ja00496a010

[29] MulQueen P, Tingey J M. Horrocks W D J. Characterization of lanthanide(III) ion binding to calmodulin using luminescence spectroscopy. Biochemistry. 1985; 24: 6639– 6645. DOI: 10.1021/bi00344a051

[30] Bentrop D. Bertini I. Cremonini M A. Forsen S. Luchinat C. malmendal A. Solution structure of the paramagnetic complex of the N-terminal domain of calmodulin with two Ce^{3+} ions by ^{1}H NMR. Biochemistry. 1997; 36: 11605– 11618. DOI: 10.1021/bi971022+

[31] Karraker. Lanthanide chemistry: From coordination in chemical complexes shaping our technology to coordination in enzymes shaping bacterial metabolism. Journal of *biochemistry* 1998; 37-2(26): 67-89.