Advances in Contemporary Research

Saccharide complexes of lanthanides

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The main focus of this review article is to bring out different aspects of interactions of saccharides with lanthanide ions. Various characteristic properties of lanthanide-saccharide complexes have been compared appropriately with those of the transition metal ones.

Introduction

Saccharides are widely distributed on earth in many different forms. These are present in various natural substances and hence belong to an important class of molecules found in biological systems where saccharide units are integrated in various ways both in the small as well as in the large molecules. These are involved in various processes, such as, storage, transport and transmission of genetic information, enzymatic reactions, and regulation of the metabolism. Saccharides and their derivatives are considered to be important not only due to their natural occurrence, but also due to their hydroxy-rich periphery, coordinating ability, homo-chirality, stereo specificity, weak immunogenicity and low toxicity. In spite of the considerable knowledge gathered regarding the metal ion—saccharide interactions in the literature, several questions pertinent to this were unanswered and this includes, binding preferences, structural and stereo-chemical features and stabilities of the species formed. This review article discusses some important aspects of metal ion complexes of saccharides in general and lanthanide metal ion complexes in particular.

Interaction of metal ions with saccharides

Complexing abilities of different saccharides are primarily dependent on two of its important properties, viz., conformation and stereo-chemistry. On the basis of the conformational analysis, it was proposed that the polyols possessing axial-equatorial-axial (ax-eq-ax) orientation or 1,3,5-triaxial arrangement (ax-ax-ax) of the hydroxyl groups provide better coordinating geometry to bind to the metal ions (Fig. 1a). Among the furanose and pyranose forms, the pyranose form can bind metal ions using its cis-as well as trans-diol arrangements, whereas the furanose form can bind only in its cis-diol arrangement (Fig. 1b). In the open chain form, saccharides tend to bind to the metal ions with a preference of three > erythro in diols, and three-three > three-erythro > erythro-erythro in triols (Fig. 1c). In addition to the conformational and stereo-chemical aspects of the saccharides, the size of the metal ion also plays an important role in effective complexation with saccharides and this happens with the metal ions having radius of 1.00–1.11 Å. The

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general trend in the stability of the complexes was found to be, $M^+ < M^{2+} < M^{3+}$. The complexation is further effective with harder metal ions due to the hard nature of the $-OH$ groups, as governed by the HSAB principles.

In 1825, the first crystalline adduct of D-glucose (D-glu) with NaCl was reported. After a gap of one and a half century, in 1971, Angyal and Davies reported metal ion interactions with neutral saccharide molecules and thereby opened new vistas of research with advanced perspectives. Later, studies on the interaction of saccharide molecules with alkali and alkaline earth metal ions were reported by research groups of Angyal and Tajmir-Riahi. Bugg and coworkers reported the crystal structure of a Ca(II)-carbohydrate complex. Till late 1980's, the work of metal-saccharide interactions was mostly confined to the alkali and alkaline earth metal ions, and the isolated solid products were all found to be "adducts" or "addition compounds", where the saccharide-$-OH$ groups were bound to the metal ions through ion-dipole interactions and not through the de-protonated hydroxyl groups to result in covalently bound alkoxo-complexes. Therefore, the interaction of metal ions with saccharides and their derivatives is considered to be a promising field in the general area of bioinorganic chemistry and hence the literature concerned with alkali and alkaline earth metal ions is being reviewed periodically.

Among various main group elements, borate complexes were the most studied based on solution conductivity and ($H$, $^{13}C$ and $^{11}B$) NMR spectral studies, where some of the complexes of polyols were found to be stabilized by intramolecular hydrogen bonds. In case of Ga(III) and In(III), formation of variable compositions were reported with D-glucaric acid. Formation of different types of Pb(II) complexes were also reported in acidic and basic media with D-glucuronic acid. Saccharides and its derivatives were used for the synthesis of adducts and complexes of Ga(III), In(III), Pb(II), As(III), Te(III) and I(III). In the past, studies of the interaction of saccharides with transition metal ions were not given much importance in the literature and those few studies reported were mainly based on the solution work. The first structurally characterized complex of a reducing sugar was the complex of the β-lyxofuranose with molybdate where the xylose was isomerized to lyxose by molybdate interaction and in the structure the pentose sugar provides an $O_6$ core for binding.

Recently Klufers et al. reported the metal ion complex of Pb(II) with D-glu which was characterized structurally. Over the past one decade, studies of transition metal ion interaction with saccharides received prominence. In this regard, our group contributed extensively to the synthesis, isolation, characterisation and solution stability studies of transition metal ions, including those of the divalent (Mn, Co, Ni, Cu, Zn), trivalent (Cr, Fe) and tetravalent (V) as well as hexavalent (Mo). Our effort in this direction was extended to the bio-interaction studies of VO$^{2+}$, Cr(III)- and Fe(III)-complexes, that includes, DNA cleavage, RNS inhibition, protein synthesis in rabbit reticulocyte lysate, Fe(III) transport through rat intestines, in vivo metallothionein induction, lipid peroxidation and cell toxicity and influence on haematological parameters. We have also reported in vitro reducing abilities of V(V), Cr(III) and Mo(VI) towards saccharides and related molecules. Though a large amount of work is known in literature, the interaction of rare earth metal ions with the hydroxyl containing molecules were not explored much. Thus, the present review focuses mainly on the contribution made by our research group towards the understanding of coordination chemistry of rare earth-saccharide complexes. Further, correlations among the data were drawn in case of lanthanide metal ion complexes as well as in case of transition metal ion complexes.
Origin and scope

It is evident from the literature that the coordination chemistry of lanthanides progressed enormously, where the ligands employed range from simple acyclic to complex macrocyclic ones. Besides the spectral and the structural characterisation of certain complexes, their chemical, photochemical and biological activities have also been addressed in the literature. As far as studies on saccharides as ligands are concerned, those with the lanthanides are extended only to a few solution interactions and these were monitored by NMR techniques. Studies in the literature are also concerned with the ability of lanthanide-saccharide complexes to act as probes in magnetic resonance imaging technique in aqueous solutions. Complexes formed between Eu(III), Ce(III) or UO$_2$$^+$$^+$ and saccharide-acids are reported in the literature. The stability constants of these complexes at low and high pH values have also been determined. Thus the saccharide interactions with lanthanide metal ions were not well recognized in the literature. In view of this, our group has recently taken up a systematic study and contributed to the development of lanthanide-saccharide chemistry which is the primary focus of this article.

Lanthanide-saccharide complexes

The complexes synthesized in this connection were shown in Fig. 3, in the form of histogram. These were generally prepared by reacting the hydrated metal halides with the di- or tetra-sodium salt of mono- or di-saccharides in 1:3 or 1:2 metal ion to ligand ratio in MeOH to result in the products in 40-75% yield. However, the Ce(III) complexes were synthesized under an atmosphere of argon to prevent aerial oxidation. The complexes were generally found to be hygroscopic and resulted in brownish pasty material when kept exposed to air for 3-4 days, but can be kept unaltered for long periods when stored under dry conditions. The lanthanide complexes were found to be less hygroscopic than the corresponding ones of the transition metal ions. The complexes are soluble in water, but insoluble in any common organic solvent.

Analytical studies

All the lanthanide-saccharide complexes yielded satisfactory results based on elemental analysis and the corresponding compositions were established as given in Table 1.
Table 1—Composition of lanthanide-saccharide complexes fitted with the formula, in case of monosaccharides, Na\textsubscript{a}M[Sac\textsubscript{a}(OH)\textsubscript{b}(H\textsubscript{2}O)\textsubscript{c}] \textsubscript{d}(H\textsubscript{2}O)\textsubscript{e} and in case of disaccharide complexes, Na\textsubscript{a}M[Sac\textsubscript{a}(OH)\textsubscript{b}(H\textsubscript{2}O)\textsubscript{c}] \textsubscript{d}(H\textsubscript{2}O)\textsubscript{e} and in case of disaccharide complexes.

<table>
<thead>
<tr>
<th>Metal ion</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ce(III)</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0-2</td>
<td>2-5</td>
<td>1-4</td>
</tr>
<tr>
<td>La(III)</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0-1</td>
<td>2-2</td>
<td>1-2</td>
</tr>
<tr>
<td>Pr(III)</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0-1</td>
<td>2-2</td>
<td>1-3</td>
</tr>
<tr>
<td>Nd(III)</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0-1</td>
<td>2-2</td>
<td>0-3</td>
</tr>
<tr>
<td>Sm(III)</td>
<td>2-3</td>
<td>2-3</td>
<td>0-2</td>
<td>0-1</td>
<td>2-2</td>
<td>0-3</td>
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<tr>
<td>Eu(III)</td>
<td>2-3</td>
<td>2-3</td>
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<td>0-1</td>
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<tr>
<td>Dy(III)</td>
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<td>2-3</td>
<td>0-2</td>
<td>0-1</td>
<td>2-2</td>
<td>0-3</td>
<td>1-8</td>
</tr>
</tbody>
</table>

*Is a dinuclear complex.*

Lanthanide-saccharide complexes were generally observed to be anionic with Na\textsuperscript{+} as counter cation. When the measured aqueous molar conductivity (ohm\textsuperscript{-1} mol\textsuperscript{-1} cm\textsuperscript{2}) was plotted against the total number of ions present in each of these complexes the plot exhibits a near linear correlation as shown in Fig. 4. The observed high saccharide-to-lanthanide ratios compared to the transition metal ion complexes is attributable to the greater affinity of saccharide ligands (oxa-donors) towards lanthanide ions, and also the high ionic potential and the ability to accommodate higher coordination numbers by these ions.

Thermal studies of these complexes showed the presence of solvent molecules, such as, acetone and or methanol along with varying number of water molecules (0 to 5). Loss of solvent molecule and degradation of the saccharide moiety were observed in 3-7 steps and total weight loss is in the range 40 to 85%. The initial weight loss is an endothermic process, observed in the temperature range, 50-150°C, corresponding to the loss of solvent molecules. Above this temperature exothermic processes were observed due to loss of CO\textsubscript{2}, H\textsubscript{2}O, and CO. End product of thermal studies was found to be oxide of lanthanide of the formula Ln_2O_3.

FTIR spectra

The FTIR spectra of the complexes exhibited broad bands characteristic of metal-bound saccharide moieties. On the other hand, spectra of simple metal ion adducts generally give sharp signals. The position, shape and width of the band observed in the range 3350-3400 cm\textsuperscript{-1} indicates the presence of water molecule and secondary interactions of saccharides through its free hydroxyl groups. Band observed in the range, 2850-2950 cm\textsuperscript{-1} is indicative of C-H stretching vibrations in all these complexes. Though a one-to-one assignment was not possible, the bands appeared in the region, 1600-1650, 1350-1450 and 1000-1100 cm\textsuperscript{-1} were assignable to δ\textsubscript{C-OH} V\textsubscript{C=O} and V\textsubscript{C=H} and V\textsubscript{C=OH} respectively. Thus the FTIR
studies have demonstrated the binding of saccharide unit to the metal ion, thereby exhibiting the complex formation.

**NMR spectra**

Resonances arising from different saccharide protons overlap to result in broad bands with multiplet structures, and thereby individual resonances could not be resolved and identified. However, the overall δ range corresponding to the skeletal protons of the saccharide molecule was found to be shifted downfield upon coordination to the metal ion. Instead, $^{13}$C NMR spectrum was found to be quite useful in structure elucidation of the complex. Representative $^{13}$C NMR spectra are shown in Fig. 5. The anomic form and the saccharide conformations were identifiable from the $^{13}$C NMR spectra. Based on the shift observed in the δ of the corresponding carbon ($\Delta\delta = $ coordination induced shift, $CIS = \delta_{\text{complex}} - \delta_{\text{liquid}}$), it is possible to identify whether the saccharide is binding in the de-protonated form (Sac-$\text{O}^-$) or in the protonated form ($\text{-OH}$) or not bound at all. Thus the preferential interaction of one oxo group of the saccharide over the other could be identified from the magnitude of down-field shift suffered by the corresponding carbon signal. While large $\Delta\delta$ (CIS) values were assigned to saccharide-$\text{O}^-$ bound to metal ion, the smaller $\Delta\delta$ values are assigned to saccharide-$\text{-OH}$ binding, indicating the difference in the binding strength of these two types. Based on CIS of the lanthanide complexes, it has been possible to identify that the aldohexoses chelate through $\text{O-3}$ and $\text{O-4}$ and provides additional coordination through $\text{OH-6}$; ketohexoses chelate through $\text{O-4}$ and $\text{O-5}$, with an additional coordination through $\text{OH-3}$; and aldopentoses interact only through $\text{O-2}$, $\text{O-3}$ and $\text{O-4}$, among which $\text{O-2}$ and $\text{O-3}$ are predicted to be involved in chelation, and the $\text{O-4}$ interacts weakly. Mode of saccharide binding to the metal ions is shown in Fig. 2. Among 60 lanthanide saccharide complexes, 55 exhibited chelation through $\text{O3-O4}$ and only four used $\text{O2-O3}$ as listed in Table 2. Thus in almost all the complexes $\text{O3}$ is exclusively involved in the coordination to metal ion in its deprotonated form (as $\text{C3-O3}$). Thus the combination of $\text{O3}$ with $\text{O2}$ or $\text{O4}$ in chelation is explainable based on the

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**Table 2**—Binding pattern of the de-protonated $\text{-OH}$ groups of saccharides to lanthanide metal ions in different lanthanide complexes

<table>
<thead>
<tr>
<th>Chelation pattern</th>
<th>Details about the complexes</th>
<th>Total number of complexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{O2-O3}$</td>
<td>$\text{Pr(III)-O-rib, Pr(III)-O-xyl, Sm(III)-O-rib, Sm(III)-O-xyl}$</td>
<td>4</td>
</tr>
<tr>
<td>$\text{O3-O4 or O3'-O4'}$</td>
<td>All mono and disaccharide complexes of $\text{Ce(III)}$ (except $\text{O-sor}$); $\text{La(III), Pr(III)}$ (except $\text{O-rib}, \text{O-xyl}$); $\text{Sm(III)}$ (except $\text{O-rib}, \text{O-xyl}$); $\text{Nd(III), Eu(III), Dy(III)}$</td>
<td>35</td>
</tr>
<tr>
<td>$\text{O4-O5}$</td>
<td>$\text{Ce(III)-O-sor}$</td>
<td>1</td>
</tr>
</tbody>
</table>

*Indicates that the chelation is through reducing part of the disaccharide
Based on the $^1$C NMR spectral studies, it has also been possible to derive that the saccharide exists primarily in the pyranose form in at least 54 compounds and in furanose form in the remaining 6. This could be attributed to metal ion induced conformational change in the saccharide molecule. It has been shown in the literature$^{99}$ that when the metal ion complex of monosaccharide is in the arabinopyranose conformation, the corresponding interaction is site specific, involving the $\text{C-3OH}$ and $\text{C-4OH}$ groups. Similar interactions were observed in case of lanthanide metal ion complexes of aldohexoses. It is also worth noting that the affinity of lectins (which has an arabinopyranose moiety) towards saccharides is sensitive to the orientations of the $\text{OH}$ groups present at $\text{C-3}$ and $\text{C-4}$. Complexes formed from disaccharides act as tridentate with additional interactions being present through $\text{-OH}$ groups. For example, while D-maltose (D-mal) can act as $\text{O-3'-O-4'-O-3}$ chelate, D-lactose (D-lac) can act as $\text{O-3'-O-4'-O-2}$ chelate. Thus the saccharide moieties in different metal ion complexes showed not only the binding of $\text{O}^-$, but also the binding of OH. Representative example of Ce(III)-mono and disaccharide complexes are shown in Fig. 6.

**Electronic spectra**

The electronic transitions in lanthanide complexes are expected to show sharp signals as the perturbation caused due to the external ligand field is minimum in case of the deep-seated $f$ orbitals. When a lanthanide ion is doped in some host lattice a large number of very sharp $f\rightarrow f$ transitions ($\Delta \lambda_{1/2} = 0.05$ to 0.2 nm) occur due to the existence of a number of microstates arising from a given $f^\text{n}$ configuration$^{99}$, but when the ion is in solution in the presence of some ligand, the number of observed transitions will be less because of the merging of some of the sharper signals to result in a broad one with larger bandwidth. Thus the band widths in lanthanide-saccharide complexes are generally broad by a factor of 100 when compared to that in the doped ions. This could be attributed to the excitation of $f$-electron to any of the higher orbital [(n+2)s, (n+2)p, (n+1)d] or may also be due to the charge transfer transitions from $\text{Sac-O--7M(III)}$.

Energy level diagram of the Pr(III) and Nd(III) are shown in Fig. 7. Thus, the solution absorption spectral bands of the complexes were broad. While Pr(III), Sm(III), and Eu(III) have all their transitions below 600 nm, Nd(III) and Dy(III) exhibit some transitions even above 750 nm. Representative spectra of La(III) - saccharide complexes are shown in Fig. 8. Similarities in the spectral features have also been observed among the lanthanide-saccharide complexes. For example, Sm(III)-complexes show similar features as that observed in case of Pr(III) and Nd(III)-complexes. Absorption band positions obtained in the case of Nd(III)-complexes have close
relevance with the features obtained in case of porphyrinato double decker complexes. UV region spectra of the complexes show bands around 260, 335, 370 nm which are characteristic of Sac-oxo→M(III) charge transfer transitions. Except in case of La(III) and Ce(III) complexes, all others show bands in the visible region arising from f→f transitions and the corresponding data including molar absorptivities is given in Table 3. Diffuse reflectance spectra of the solid lanthanide-saccharide complexes showed broad bands at the same position as that observed in solution. Thus the study indicates the retainment of the solid-state structure upon dissolution.

Circular dichroism
Circular dichroism spectra of all the complexes in aqueous solution exhibited bands in the range, 215-400 nm. Though the Cotton effect is not very prominent in most of the disaccharide complexes, the sign of the CD curve was found to be similar to that of the mono-saccharide complexes. The spectral results indicate similarities in the configuration around the metal center in all these complexes. Some general features observed are as follows: among the aldohexoses, complexes of D-galactose (D-gal) showed opposite sign compared to the complexes of D-glu and D-man, whereas, the complexes of keto-hexose have shown CD band with same sign. But in
Thus, the study revealed that the oxidation state of the Sm(I)Ce(II) ion using appropriate accordance with those reported in the literature.

The observed and the calculated values in the saccharide complexes exhibited different variation observed between the experimental and the mcasurcment corresponding metal ion complex.

The coordination sphere is different, this leads to a difference in the sign of CD spectra. Thus, the spectral analysis of these complexes very well indicated difference in the orientation of a particular saccharide moiety in the corresponding metal ion complex.

**Magnetic studies**

Room temperature magnetic susceptibility measurement of the solid products of lanthanide - saccharide complexes exhibited different \( \mu_{\text{eff}} \) values. The observed and the calculated \( \mu_{\text{eff}} \) values of lanthanide complexes are given in Table 4. Ce(III) and Sm(III) complexes showed \( \mu_{\text{eff}} \) values in the range 2.05-2.62 and 1.03-1.85 BM respectively, whereas, Pr(III) and Nd(III) complexes showed 3.30-3.95 BM. The magnetic moment was calculated for Ce(III) ion using appropriate \( \mu \) expression. The variation observed between the experimental and the calculated \( \mu_{\text{eff}} \) values in case of Ce(III) complexes is attributed to the presence of a mixture of compounds in different oxidation states. Whereas in the case of Sm(III)-complexes, the \( \mu_{\text{eff}} \) observed are in accordance with those reported in the literature. Thus, the study revealed that the oxidation state of the metal ion in all the complexes is +3. Comparison of the calculated \( \mu_{\text{eff}} \) with that of the observed shows good agreement except in case of Sm(III) and Eu(III) complexes that may be due to the smaller energy gap present between the different energy levels, and as a result the first, second and third excited energy levels getting more populated.

**Data correlations and proposed structures**

Spectral techniques, such as, FTIR and absorption spectra have demonstrated the direct binding of the saccharide moieties with M(III) lanthanide ions. Both the LMCT and the \( f-\gamma \) transitions were characteristic of the complexes formed. The CD spectra demonstrated the dissymmetry present around the metal ion center in the field of saccharide moieties. On the other hand, the thermal degradation experiments (TGA and DTA) revealed the presence of H_2O and/or solvent molecules and the total loss of organic moiety present in the complexes. These studies also elicited the fragmentation pattern.

However, the \( ^{13} \text{C} \) NMR studies delineated the binding of specific o xo (-O) and/or hydroxy (-OH) groups to the metal center. Such NMR based assignment took advantage of the magnitude of coordination induced shift, CIS (\( \Delta \delta \)) in various carbon centers and also that of the orientation of the adjacent hydroxyl groups present in the corresponding saccharide moiety, whether such -OH groups are capable of forming a chelate or not. If the single 4f electron of Ce(III) were to be shifted to 5d, one would expect concomitant changes in the absorption spectra and also in the magnetic susceptibility measurements. Though the \( \mu_{\text{spin}} \) was found to be higher than the spin-only value, it is certainly lower than the expected value of 2.49 BM, which includes the total contribution of spin-orbit coupling. If the d-character was to be considered, a lowering of spin-orbit coupling is expected.

The molar conductance values for mono-saccharide complexes are observed in the range 160-200 ohm^{-1} mol^{-1} cm^{2}, whereas those of the disaccharide complexes are in the range of 50-90 ohm^{-1} mol^{-1} cm^{2}. The conductance data suggests a 1:1, 1:2 and 1:3 electrolyte behavior in different complexes and the data correlates fairly linear with the number of ions present in the complex as shown in the Fig. 4. Thus the data supports the presence of a tri-negative complex anion of the formula \([\text{M(O-Sac)}]^{3-}\) for mono-saccharides and a mono-ionic core of the

<table>
<thead>
<tr>
<th>Metal ion</th>
<th>No. of electrons</th>
<th>( \mu_1 ) (calculated)*</th>
<th>( \mu_1 ) (obseerved)***</th>
</tr>
</thead>
<tbody>
<tr>
<td>La(III)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ce(III)</td>
<td>1</td>
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<td>2.05-2.62</td>
</tr>
<tr>
<td>Pr(III)</td>
<td>2</td>
<td>5.58</td>
<td>3.30-3.95</td>
</tr>
<tr>
<td>Nd(III)</td>
<td>3</td>
<td>3.62</td>
<td>3.40-3.83</td>
</tr>
<tr>
<td>Sm(III)</td>
<td>6</td>
<td>0.84 (1.5-1.6)**</td>
<td>1.03-1.83</td>
</tr>
<tr>
<td>Eu(III)</td>
<td>6</td>
<td>0 (3.4-3.6)**</td>
<td>3.06-3.65</td>
</tr>
<tr>
<td>Dy(III)</td>
<td>9</td>
<td>10.63</td>
<td>9.98-10.93</td>
</tr>
</tbody>
</table>

*Calculated using the expression \( g[J(J+1)]^{1/2} \) BM where \( J \) is for the ground state level and \( g = 1 + [(J(J+1)+S(S+1)-1)/(2J(J+1))]^{1/2} \).

**Over different saccharide complexes of the same metal ion**

Table 4—Magnetic moment data for lanthanide - saccharide complexes.
formula \([\text{M(di-Sac)(OH)(H}_2\text{O})_2]\) for disaccharides. Elemental analysis data agrees well with our proposed composition of the complexes. Proposed structures of some representative mono- and di-saccharide complexes of La(III) are shown in Fig. 9.

In case of the rare earth metal-saccharide complexes the coordination numbers are generally seven (Sm(III), Eu(III) and Dy(III)), eight (La(III), Sm(III), Eu(III) and Dy(III)) and nine (Ce(III), Pr(III), Nd(III) and a few Sm(III), Eu(III) and Dy(III) complexes) with the geometry proposed being pentagonal bipyramidal, bi-capped octahedron or bi-capped trigonal prism, and tri-capped trigonal prism, respectively.

Presence of nine coordination in Pr(III)- and Nd(III)-complex is supported by single crystal XRD studies of the corresponding D-rib complex, as shown in Fig. 10. Out of the nine ligation, eight were through oxygen atoms (three from D-rib and five from water molecules) and ninth one was through chloride. The saccharide provides an ax-ax-ax orientation and retains its chair conformation, in the complex. Similar structural characteristics were observed in case of Nd(III)-D-galactitol complexes. Both the complexes exhibited extensive hydrogen bond interactions using \(-\text{OH}, \text{H}_2\text{O}\) and \(\text{Cl}^\text{-}\) groups. It has been noted in recent literature that Eu(III) binds with two molecules of cyclohexanetriol as tridentate along with one or two chelating nitrates and water molecules to crystallize predominantly to give a nine-coordinated, tri-capped trigonal prismatic complex. Representative examples of mono- and di-saccharide complexes of Sm(III), Eu(III) and Dy(III) are shown in Figs 11 and 12 respectively. It has been found in the literature that mono-saccharides act as tri-dentate and di-saccharides act as tetra- or penta-dentate ligands in the complexes of lanthanide ions, however, these act...
as bi- or tri-dentate ones in case of transition metal ion complexes.

Structurally similar Pr(III)-D-rib and Nd(III) complexes show tridentate mode of binding as shown in Fig. 10 in case of 1:1 complex. However, in our studies while the mono-saccharides exhibited complexes with 1:3 ratio, those of di-saccharides exhibited 1:1 complex as shown in Fig. 13.

Conclusions

Saccharides are building blocks of a number of biological molecules, including small and large ones. These systems drew the attention of scientists, with diverse interests, from all over the world. By their chemical nature, these can act as potential molecules for interacting with metal ions. Though this review addresses various aspects related to the metal ion-saccharide interactions especially of lanthanide ones, the coordination chemistry of saccharides is still found to be in its infancy stage. Based on several spectral and analytical techniques, structure and binding aspects of lanthanide-saccharide complexes were established. Primary aim of this article is to highlight the synthesis and characterization of saccharide complexes of trivalent lanthanide ions. The lanthanide-saccharide complexes have shown structural diversity among them as given in this review (Figs 6, 9, 11-13). Molecular composition (in terms of ratio), coordination number, presence of solvent molecules, and conformation of the saccharide moiety are described based on different spectral and analytical techniques.
Recent developments and future projections

Presence of saccharide moieties in biological systems provide impetus for the growth of the field of metal ion–saccharide interactions. Recent trends in this field include the development of synthetic methodologies followed by characterization. In this context, the recent literature deals with the synthesis, isolation, characterization and bio-interaction studies of a number of transition metal ions with simple saccharides and their derivatives. Biointeraction studies, such as, DNA cleavage,\(^{50,64}\) RNase inhibition,\(^{65}\) protein synthesis in rabbit reticulocyte lysate,\(^{66}\) Fe(lll) transport, in vivo metallothionein induction,\(^{99}\) lipid peroxidation and cell toxicity were performed and putative interactions of transition metal–saccharide complexes is reported. Studies reveal that these complexes have some biological significance and promise to be potentially useful in medicine and even in clinical trials. In spite of all these developments it is still correct in saying that the studies of metal ion–saccharide interactions is largely unexplored.

Due to the fact that the saccharides undergo easy isomerisation and conformational changes, its complexation with metal ion results in the formation of mixture of products, hence researchers are reluctant to take up this particular field of research. During the past several years researchers are putting constant efforts to develop methodologies to crystallize metal ion-saccharide complexes. Attempts to circumvent this resulted in the development of protecting group, anchoring group and N-glycosylation strategies. The results were encouraging with the report of a number of crystallized metal ion-complexes of protected saccharides in the recent literature\(^{101-105}\) and our group is contributing substantially to the synthesis, characterization and solution behavior of saccharides and its derivatives including N-glycosyl amines\(^{117-120}\) and its metal ion complexes\(^{21-26}\).

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