1.1 Introduction:-

The importance of coordination compounds, playing different roles, in living systems is well established. The studies on coordination complexes have become a challenge to the present day chemist [1]. Coordination chemistry in a broad sense constitutes a major part of inorganic chemistry. The field of coordination chemistry has always been a challenge to chemists and has become a fast emerging area of chemistry [2]. The rapidly developing field of bio-inorganic chemistry is centered on the study of coordination compounds present in living systems. Many biologically active compounds are complexes, and even the similar types of complexes have served as model compounds in investigation of bodily processes. In fact, the new field of bio-inorganic chemistry is concerned largely with coordination chemistry.

The complexes which are found in minerals, plants and animals are of great significance because they exhibit important functions in the environment where they are present. The synthesis of newer and newer organic chelating agents that can coordinate with transition metal ions has tempted the researchers to synthesize more and more coordination complexes. The rapid development in the field of bio-inorganic chemistry is centered on the study of coordination compounds present in living systems.

A complex defined by Rossoitti and coworkers [3] is a species formed by the association of two or more simple species, each capable of independent existence. When one of the species is a metal ion, the resulting entity is known as a metal complex. The term ‘ligand’ is applied to the particular molecule or ion attached to the central metal ion [4]. Some ligands are attached to central metal ion by more than one atom in such a manner to form a ring. This is known as chelation and the resulting complex is called as metal chelate [5]. The stability of chelate depends on the size of the ring. Generally coordinated compounds of a saturated five membered ring are more stable than those formed of unsaturated five membered rings. However, a great stability to metal chelate is achieved with the formation of six membered ring [6].

The modern studies of co-ordination compounds begins with Alfred Werner. Alfred Werner’s classical idea of coordination bond, in 1893, gave a great deal to the development of coordination chemistry [7]. The theory postulated that in coordination compounds, the metal exhibits two types of valencies, primary and secondary. The primary valency is ionisable and non-directional, where as secondary valency is non
ionisable and directional. The bonds between the ligand and the metal ion are due to the secondary valencies of metal ions. The development of electronic theory of valency by Lewis, Kossel, Langmuir, Sidgwick, Fajan and coworkers [8], cleared the ideas regarding primary (oxidation state) and secondary (co-ordination number) valencies in complexes.

In 1931, Pauling gave valence bond theory (VBT), which is based on revolutionary idea of hybridization of atomic orbitals [9]. According to this theory, the central metal ion makes available number of empty s, p, d hybrid orbitals equal to its coordination number. These orbitals undergo particular type of hybridization such as sp, sp$^2$, sp$^3$, dsp$^2$, d$^2$sp$^3$ and sp$^3$d$^3$ which gives shape to the molecule as linear, trigonal, tetrahedral, square planer and octahedral respectively. The filled ligand orbitals overlap with empty hybrid orbitals of metal ions to form coordinate covalent bond. This theory explains mainly electronic structure of central metal ion, shapes of complexes, magnetic properties of complexes and stereochemistry. However, it does not give proper explanation of maximum pairing, the spectra of the complexes and quantitative interpretation of magnetic properties.

Crystal field theory (CFT) developed by Bethe [10] in 1929, originally applied to crystalline solids was further developed by Van Vleck [11] and coworkers. According to this theory, the bond between metal and ligand is neither due to sharing of electron nor due to interaction of atomic orbitals. The bond between metal and ligand is purely electrostatic. The interaction of d-orbitals of central metal ion with the surrounding ligand orbitals produces crystal field effect. The electric field due to the ligands lifts the degeneracy of the five d-orbitals of central metal ion and splits them into two energy sublevels t$_2$g-triplet and eg-doublet. The energies of these sublevels depends upon the type of geometry and nature of ligand. The energy difference between t$_2$g and eg levels is known as crystal field stabilization energy and is denoted by 10D$q$. The magnitude of 10D$q$ depends upon the nature of ligand and charge on the central metal ion. CFT interprets the magnetic and spectral properties of transition metal complexes quantitatively.

The molecular orbital theory, developed by Van Vleck [11], although more complicated than the VBT and CFT theories, explains more satisfactorily the nature of bonding involved in coordination complexes. The formation of covalent bond with
metal ion and donor group is occurred due to with or without replacement of hydrogen atom from an organic functional group.

An enzyme provides an arrangement of side-chain functional groups having an appropriate sized hole with the preferred groups on enzyme side chains needed to bind the required metal ion. The optimal number of such binding groups is chosen for the particular metal ion, together with the appropriate hydrophobic or hydrophilic environment in the binding site. Metal ions may be bound by main-chain amino and carbonyl groups, but specific binding is achieved by the amino acid side chains, particularly the carboxylate groups of aspartic and glutamic acid, and the ring nitrogen atom of histidine. Other side chains that bind metal ions include tryptophan (ring nitrogen), cysteine (thiol), methionine (thioether), serine, threonine, tyrosine (hydroxyl groups), and asparagine and glutamine (carbonyl groups, less often amino groups). Each ligand contains at least one functional group which may coordinate to metal ion through it. Depending on the functional group coordinating to the metal ion, they are classified as Schiff bases, β-diketones, hydrazides, semicabazones, 8-hydroxyquinoline etc.

1.2 Importance of macrocyclic ligands:

Macrocycles are important and powerful ligands, ubiquitous in transition metal coordination chemistry for the following reasons: 1) They mimic important biological ligands developed long ago by nature, for example the porphyrin prosthetic group of many metalloproteins. 2) They impart thermodynamic and kinetic stabilities to their metal complexes uncommon or non-existent with ligands of lesser types. Obviously, the question arises what exactly this macrocycle is? For the coordination chemists, good working definition of macrocyclic ligand is, “a cyclic molecule with three or more potential donor atoms in a ring of at least nine atoms.” This is about a cyclic molecule but macrocyclic ligand should contain donor atoms, which may form coordinate bond with metal centers.

During the past few decades there has been a great deal of activities in the field of macrocyclic chemistry. The coordination behavior of macrocyclic ligand is no different in principle from that of open chain polydentate ligands, although in practice, the unusual and often unexpected properties of the systems justify their, being given special treatment. An important class of macrocyclic ligand consists of macrobicyclic polyaza, polyoxa ligands.
The increased thermodynamic stability of macrocyclic complexes over their linear analogs having the same number of chelate rings is known as the macrocyclic effect, the kinetic macrocyclic effect refers to the slow kinetics of dissociation of macrocyclic compounds as compared to the open chain analogs. A macrocyclic ligand is a cyclic compound with nine or more members including all the heteroatoms and with three or more donor atoms. These donor atoms are usually positioned so that upon coordination preferably five or six membered chelate rings are formed with the metal ion. The number of atoms in the macrocyclic ring determines the macrocyclic cavity size. The cavity size is also affected by the backbone rigidity and by the nature and the type of hybridization of the donor atom. Unsaturation in the macrocyclic ring can have significant effects. Transition metal porphyrin complexes possessing oxo (-O), imido (-NR), and carbene(-CR₂) ligands are of interest as potential models for biological processes and as possible reagents for organic synthesis. Of special interest is the use of these complexes as reagents to affect alkene epoxidation, aziridination and cyclopropanation reactions, respectively. In addition, the chemistry of triazamacrocycles, N-functionalized with hard ligators, e.g. carboxylic acids [12-13], alcohols [14], amines [15], sulfates [16], phosphates [17], imidazoles [18], and pyridine [19] is now well established. More recently the chemistry has been extended to include more classic soft donors such as sulfides [20], alkenes [21], phosphenes [22,23] and alkynes [24,25].

Extensive unsaturation results in the loss of flexibility, which in turn may lead to increased inertness of the complex. Based on donor atoms type, macrocyclic ligands can be classified as crown ethers (Oxygen donor atoms), polyaza macrocycles or azacrown ethers (Nitrogen donor atoms), macrocycles containing Sulphur, Phosphorus, Arsenic atoms and macrocyclic ligands with mixed donor atoms (polyaza polyoxa macrocycles, lariat ethers). Macrocycles with pendant functional groups include polyaza macrocycles that have coordinating side arm’s attached to the nitrogen. These include NOTA, DOTA, DOTMA, TETA (acetate side arms). These ligands are capable of axial metal ion coordination. Chelation will be more efficient because the donor atoms are held near to the central metal ion. Synthesis of macrocyclic compounds have been known for over 75 years, although a genuine spate of publication in this area started in the late 1960s. In this period, more than 5000 macrocyclic compounds were reported, and then their number has increased markedly.
from year to year. It is, of course, impossible to provide an exhaustive survey of these compounds within the framework of this chapter. To organize the data consideration logically, we have chosen the type of donor heteroatoms as a classificatory attribute, therefore, the sequence of presentation is as follows.

1.2.1 Oxygen-containing macrocyclic compounds:-

1.2.1.1 Polyoxacycloalkanes (Crown ethers) :-

18-Crown-6 (18 C₆), the best known of the crown ethers, was obtained for the first time by Pedersen in 1967 [26]. The cyclization of an open-chain precursor yielded only 1.8% of the crown ether (Fig 1.1).

![Fig. 1.1](image1)

One may introduce substituents into crown ether molecule for several purposes. Thus, alkyl groups especially long chain ones (C₈ and longer) have markedly increased the lipophilicity of macrocycles. Such substituents as the cyclohexane group are introduced into macrocyclic molecules for the same purpose. In addition, the cyclohexane group improves the solubility of macrocycles in organic solvents. The substituents that are capable of additionally coordinating to metal ions (such as etheric fragments or carboxyl groups) produce so-called Lariat Ethers. Dicyclohexano 18-C-6 (Fig.1.2) is the most renowned compound among the substituted crowns obtained from catalytic hydrogenation of dibenzocrown ethers.

![Fig. 1.2](image2)
1.2.2 Nitrogen-containing macrocyclic compounds:-

1.2.2.1 Aza crowns:-

The class of aza crowns is the largest and most diverse in the realm of macrocyclic compounds. This is because nitrogen-containing groups, in contrast to those containing oxygen, may be of quite various types; nitrogen atoms may be included in secondary and tertiary amino, azomethyno, pyrrolo, pyridine, ammonium, and other groups moreover, the nitrogen of all these types may occur in some macrocyclic compound. Nitrogen atoms may also be included in macrocyclic fragments of thiourea, guanidine, amide, hydrazo and azo compounds.

1.2.2.2 Macroyclic polyamines:-

The most prominent representative of this class of macrocyclic compounds, 1,4,8,11-tetraazacyclotetradecane (cyclam) (Fig.1.3) was first obtained by interaction of polyamine with 1,3 dibromopropane with a yield of only 1.5% [27].

![Fig.1.3](image)

1.2.2.2 Oxaazacrown compounds:-

Aliphatic oxaazacrown compounds are typically prepared either by creating C-O bonds or by Richman –Atkins method using oxygen containing α,ω - diamines. For example, benzooxaazacrown compounds obtained from cycloalkylation of o-aminophenol (Fig.1.4) [28].

![Fig.1.4](image)
1.2.3 Sulphur containing macrocycles:-

1.2.3.1 Thiacrowns:-

The number of known thiacrowns falls far short of the number of oxygen containing macrocycles, for instance this might be because there is no pronounced template effect of any metal in the chemistry of thiacrowns and therefore, synthesis of macrocycles in question is quite complicated. The synthesis of thiacrowns generally requires conditions of high dilution and yields of the desired compounds are rather poor.

1.2.3.2 Macrocyclic polythia-ethers:-

Under high dilution conditions, the reactions of α,ω-dithiols and dihalogenoalkanes in the presence of bases yields thiacrowns, e.g. (Fig. 1.5) and related compounds [30]. Thia-18C₆ (Fig. 1.6) was prepared by several researchers [24,25,29-32].

![Fig. 1.5](image1)

**Fig. 1.5**

![Fig. 1.6](image2)

**Fig. 1.6**

1.2.3.3 Oxa thiacrowns:-

About 20 aliphatic oxathiacrowns are now known. Virtually all of them were prepared by the interaction of α,ω-dithiols and oligoethylene chlorides [33,34] for example, oxathiacrown compounds (Fig. 1.7).

![Fig. 1.7](image3)

**Fig. 1.7**
1.2.3.4 Thiaazacrowns:

Several synthetic approaches for constructing thiaazacrowns have also been reported. For example, interaction of bis (2-bromoethyl) amine with ethanedithiol proceeds like a 2:2 condensation, yielding compounds (Fig. 1.8) [35].

![Fig. 1.8](image_url)

The coordination chemistry of macrocyclic ligands is a fascinating area of research. The synthetic, kinetic and structural aspects [36,37] of polyazamacrocyclic complexes have received considerable attention and a variety of such systems have been synthesized [38-40].

The polyazamacrocyclic complexes, particularly those of tetraazamacrocycle along with the pentaaza and higher polyazamacrocycles, have been widely studied in view of their potential for binding more than one metal ion [41,42]. The relationship of electronic properties and reactivity of these synthetic macrocyclic complexes to those of naturally occurring macrocycles, such as porphyrins [43] and corrins, continues to promote great interest in their design and preparation.

Metal complexes with synthetic macrocyclic ligands are of huge significance, in part because of their resemblance with many natural systems, e.g. porphyrins and cobalamines. The publication of several review articles and books covering a variety of aspects of synthetic macrocyclic ligands divulge the great importance attached to them [44-46]. Due to importance in biological systems, as a synthetic model for many metalloenzyme reactions [47,48], their novel structural features and extraordinary magnetic properties, has created substantial interest in the transition metal chemistry in the mixed ligand compounds during last few years [49-53]. Recently, the macrorcyclic complexes of both transition and non transition elements have received considerable interest due to their wide diversity in chemical [54-56] and biological [57,58] systems.
One of the interesting aspects of macrocyclic complex is the influence of stereochemical preferences of a particular metal ion, ligand conformation and in turn, the capacity of metal ion to accommodate the geometrical constraints imposed by the macrocycle. An important property of both naturally occurring and synthetic macrocycles having varying degrees of unsaturation is their ability to stabilize both high and low oxidation states of the metal ions in the metabolic functions of naturally occurring porphyrins.

In the macrocyclic complexes, metal ion is placed at the center of cyclic environment of molecules like cryptates, crown ethers, macrolides, cyclic peptides. Schiff bases have triggered a great deal of interest in their synthesis, structure and reactivity. They have an ability to encapsulate metal ions with remarkable specificity and stability.

Synthetic macrocycles is a growing class of compounds with varying chemistry [59-62] Viz. donating atoms, ring size and type of reaction. The chemical properties of macrocyclic complexes can be tuned to force metal ions to adopt unusual coordination geometry. Transition metal macrocyclic complexes have received much attention as an active part of metalloenzymes [63] and as biomimic model compounds [64,65] due to their resemblance with natural proteins like hmyerthrin and enzymes. The complexes of this type are also useful in catalysis [66,67]. The synthesis and characterization of the coordination compounds with azamacrocyclic ligands has evolved the great attention during the last few years [68,69]. Additional information related to the spectroscopic properties of these ligands and their coordination compounds is able to generate novel sterochemical, elecrochemical and electronic properties along with the exploration of biological activity [70].

1.3 Applications of macrocyclic compounds in various fields:-

Coordination chemistry of macrocyclic ligands has been a fascinating area of current research interest to the inorganic chemists all over the world. The continued interest and quest in designing new macrocyclic ligands stem mainly from their use as models for protein-metal binding sites in a substantial array of metalloproteins in biological systems, as synthetic ionophores, as models to study the magnetic exchange phenomena, as therapeutic reagents in chelate therapy for the treatment of metal intoxication, as cyclic antibiotics that owe their antibiotic actions to specific
metal complexation, to study the guesthost interactions, and in catalysis. Recognition of the importance of complexes containing macrocyclic ligands has led to a considerable effort being invested in developing reliable inexpensive synthetic routes for these compounds [71-74]. Several classes of macrocyclic ligands, such as saturated polyazamacrocycles, imine Schiff base macrocycles, oxazolidine-containing macrocycles, polyoxamacrocycles, polyoxaazamacrocycles, polyoxa- and oxaaazacoronands, crown ethers, lariat crown ethers, cryptands, cavitands, calixarenes, carcerands, cyclodextrins, cryptophanes, cyclophanes, hemispherands, catenanes, podands, compartmental macrocyclic ligands which form homo and heterodinuclear complexes, structurally reinforced macrocycles, redox responsive macrocycles, photoresponsive macrocycles, pH-responsive macrocycles, chromogenic macrocycles, siderophores and macrocycles containing pendant arms have been synthesized. These macrocycles which contain varying combinations of aza (N), oxa(O), phospa (P), and sulfa(S) ligating atoms can be tailored to accommodate specific metal ions by the fine-tuning of the ligand design features, such as the macrocyclic hole size, nature of the ligand donors, donor set, donor array, ligand conjugation, ligand substitution, number and size of the chelate rings, ligand flexibility, and nature of the ligand backbone. The different types of macrocyclic ligands are particularly exciting because of the importance in generating new areas of fundamental chemistry and many opportunities of applied chemistry. The majority of macrocycles represent creative and focused efforts to design molecules which will have particular uses.

The lanthanide complexes find extensive applications in technology, industry and medicine [75]. They are widely used in separation of lanthanide ions by ion exchange, solvent extraction and gas chromatography [80]. Few Europium complexes have received much attention as laser materials [81]. Few of the lanthanide complexes are commonly used as NMR shift reagents [82] to make the spectra more clear and simple so that information regarding the structure can be drawn very easily. The complexes of optically active β-diketonates find extensive application in assigning the purity of optical isomers [83]. Besides, some β - diketonets complexes have been shown to be good substitutes for tetraethyl lead, the antiknock additive for gasoline. Together with triethyl aluminium, some lanthanide complexes are used as Ziegler-Natta catalyst for 1-4 stereospecific polymerization of butadiene [84]. Some carboxylate complexes of lanthanide are used as antioxidant in the chelation therapy
to remove of $^{144}$Ce contamination in the body [85]. In addition to this, several lanthanide complexes are found to possess antifungal, antibacterial, antiviral, anticoagulant, anticancerous and antipesticidel properties [75-79]. It has also been found that the toxicity decreases with chelation [86] and hence the lanthanide complexes derived from ligands capable of forming chelates are of great importance.

The ability of the Ln(III) metal ions to promote the Schiff base condensation of the appropriate diamine and dicarboxyl precursors, resulting in the formation of metal complexes of otherwise inaccessible macrocyclic ligands, is well established [87,88]. Macrocyclic ligands form stable complexes with lanthanides and actinides and hence they serve as a springboard to explore the coordination chemistry of these metal ions. Macrocyclic complexes of lanthanides are currently attracting much attention as radio-pharmaceuticals [89], in radioimmunotherapy [89-94], in other medical applications, such as radioimmunoscintigraphy (y-cintigraphy) [95,96] and positron emission tomography [97,98], as contrast-enhancing agents in magnetic resonance imaging [99-107], as NMR shift reagent [108-115], as NMR shift and relaxation agents for proteins [116,117] and biological cations [110,113,118], as fluorescent probes in fluoroimmunoassay [119-123] and in other clinical applications [123], as luminescent labels in luminescence immunoassay [124], as luminophores,[119,120] and as luminescent probes and luminescent concentrator [120]. Luminescent lanthanide complexes of chelating ligands have been suggested as markers in cytology and immunology and may serve as luminescent biomarkers [125]. Lanthanide luminescent probes [122,126-129] are extensively used for studying metal ion sites in macrocyclic complexes [130,131] and in biological systems [122,130]. There is an emerging interest in the application of macrocyclic ligands as effective metal ion chelator [132-139] and in the separation of lanthanides [140-144]. One of the most tantalizing applications of Ln(III) macrocyclic complexes is the efficient catalytic cleavage of RNA (transesterification of RNA) [145-147]. Homodinuclear lanthanide complexes are used to study the nature and application of lanthanide metal-metal interactions in lasers [148,149] and phosphors [150,151], to characterize complex biomolecules [127,130], to determine the metal-metal distances [152], the local coordination symmetry [130] in bio- molecules and to determine the depth of the active sites from protein surface [153-155]. Dinuclear Ln(III) complexes are also important as novel tunable photonic devices [156] with potential application.
in biomedical diagnostics [157] and fluorescence imaging [157,158]. Possible applications of immobilized dinucleating chelates for the efficient separation and purification of the lanthanides are of great interest [159,160]. Dinuclear lanthanide complexes are also important in studying the molecular recognition processes which govern the Ln (III) cations pairing events [161].

1.4 Literature survey of previous related studies:

Lanthanum and next fourteen elements which follow it are called Lanthanides. In the last two decades, there has been rapid growth in the field of coordination chemistry of lanthanides with multidentate ligands [162,163]. Due to the wide variety of potential applications in biology, medicine and material science, some of the lanthanide complexes are increasingly used as diagnostic tools in biomedical analysis as responsive analytical systems [164,165]. The biological properties of the lanthanides, primarily based on their similarity to calcium, have been the basis for research into potential therapeutic applications of lanthanides since from the early part of the twentieth century [166,167]. The lanthanides (for convenience abbreviated to Ln) is a group of elements from lanthanum (Z = 57) to lutetium (Z = 71). Though originally described as “‘rare earths”’ because of their natural occurrence as metal oxides, they are not particularly rare. With similar ionic radii to calcium, but a higher charge, the Ln(III) ions have a high affinity for Ca(II) sites on biological molecules and hence can act as either Ca(II) inhibitors or probes.

Lanthanides and actinides form complexes of higher coordination numbers ranging from 7 to 12. This is attributed to the large size of these metal ions together with the ionic nature of the metal-ligand bonding. Studies on the involvement of f-electrons in metal-ligand bonding constitutes a challenging objective to be vigorously pursued. There is a need for synthesizing stable macrocyclic complexes of f-block metal ions to explore the bonding parameters and to tap their potential uses. The challenge is to design macrocycles with appropriate ligand design features required to form stable complexes. The rational design features for tailoring such macrocycles require a more detailed understanding of the subtle factors underlying the influence of structure and dynamics of the ligand on the stability of complexes.

Bhowon et al. [168] reported metal chelates of bidentate schiff bases derived from N-(2-pyrrolylmethylene)-2-aminophenol. These were synthesized and characterized by elemental analysis, conductivity measurement, magnetic
susceptibility, UV-visible, FTIR, $^1$H-NMR spectra and thermal analysis study (Fig. 1.9).

Mohanan and coworkers [169] studied Ln(III) complexes of tridentate ligands with NNO as donor atoms and showed that the complexes possessed 1:2 metal-ligand ratio. X-ray diffraction studies on the ligand and [La(HSAT)$_2$Cl$_3$] showed that the ligand exists in tetragonal and the complex in orthorhombic crystalline form. Thermal decomposition study of La(III) complex was carried out. The complex [La(HSAT)$_2$Cl$_3$] underwent facile transesterification. The ligand and the complexes were screened for their antibacterial activities (Fig. 1.10).

La(III), Sm(III), Eu(III) and Tb(III) complexes of tetradeinate schiff bases are reported by Singh and coworkers [170], which are synthesized and characterized by various physico-chemical techniques. Mass spectrum explains the successive degradation of the molecular species in solution and justifies ML complexes. Vibrational spectra indicate coordination of Ln(III) with amide and carboxylate oxygen of the ligand along with nitrate ions. The magnetic moment of Sm(III) and Eu(III) complexes showed slightly higher-values originated due to low J-J separation leading to thermal population of next higher energy J levels and susceptibility due to
first order Zeeman effect. The strong luminescence emitting peaks at 587 nm for Eu(III) and 543 nm for Tb(III) were observed and attributed to the ligand having an enhanced effect to the luminescence intensity of the Eu(III) and Tb(III). The thermal behaviour of complexes showed the loss of water molecules and nitrate ion in first step followed by the removal of two molecules of nitrate ions and then decomposition of the ligand molecule in subsequent steps. Kinetic and thermodynamic parameters were computed from thermal data using Coats and Redfern methods, which confirmed first order kinetics. The \( \mu_{\text{eff}} \) values of 3.8-4 B.M. and ESR spectral data indicated that the complexes have tetrahedral geometry. The proposed structure for these complexes is presented in (Fig.1.11).

![Fig.1.11](image)

Chandra et al. [171] reported lanthanide complexes derived from hexadentate macrocyclic ligand. The ligand was characterized by elemental analyses, IR, Mass, and \(^1\)H NMR spectral studies. All the complexes of La\(^{3+}\), Ce\(^{3+}\), Nd\(^{3+}\), Sm\(^{3+}\) and Eu\(^{3+}\) were characterized by elemental analyses, molar conductance measurements, magnetic susceptibility measurements, IR, Mass, electronic spectral techniques and thermal studies. On the basis of absorption spectra, the different parameters i.e. nephelauxetic ratio, covalency factor, Sinha parameter and covalency angular overlap parameter for Nd(III) and Sm(III) were calculated. The values of these parameters suggest the metal–ligand covalent bonding. Except La(III), all the complexes are paramagnetic in nature. The thermal studies reveal the presence of coordinated water molecule. All the complexes were found to have coordination number nine. On the basis of above spectral studies the following structure may be suggested for the complexes (Fig.1.12).
Gregolinski et al. [172] reported lanthanide complexes of 2 + 2 meso type macrocycle derived from trans-1,2-diaminocyclohexane and 2,6-diformylpyridine: X-ray crystal structures of La(III) and Sm(III) complexes. The [LnL](NO\textsubscript{3})\textsubscript{3}. nH\textsubscript{2}O complexes of the series of all lanthanide(III) ions, except radioactive Pm, with the meso-type hexaazamacrocycle L, derived from racemic trans-1,2-diaminocyclohexane and 2,6-diformylpyridine, have been synthesised and characterized. The X-ray crystal structures of the isomorphic La(III) and Sm(III) complexes show that the Ln(III) ions are coordinated by six nitrogen atoms of the relatively flat macrocycle L as well as by two axial bidentate nitrate anions and methanol molecule. The complexes have been characterised by NMR and mass spectrometry. \textsuperscript{1}H NMR signals of the Ce\textsuperscript{3+}, Pr\textsuperscript{3+}, Nd\textsuperscript{3+}, Eu\textsuperscript{3+} and Yb\textsuperscript{3+} complexes have been assigned on the basis of the COSY and HMQC spectra, and for the remaining lanthanide complexes the signals were assigned on the basis of linewidths analysis. The paramagnetic shifts of the series of lanthanide complexes [LnL](NO\textsubscript{3})\textsubscript{3}. nH\textsubscript{2}O have been analysed using both crystal-field dependent and independent methods. The results of this analysis indicate a change of coordination number along the series of Ln(III) complexes. The properties and stability of the Ln(III) complexes of the macrocycle L have been compared with those of the isomeric chiral macrocycle L\textsubscript{1} (Fig.1.13)
Shelke et al. [173] reported synthesis and characterization of tetradeutate N₂O₂ schiff base ligand and its rare earth metal complexes. The solid complexes of La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) with 4-hydroxy -3-(1-\{2-(2,4-dihydroxybenzylidene)-aminophenylimino\}-ethyl)-6-methyl-pyran-2-one (H₂L) derived fromo-phenylenediamine,3-acetyl-6-methyl-(2H)pyran,2,4(3H)-dione dehydroacetic acid or DHA) and 2, 4-dihydroxy benzaldehyde have been synthesized and characterized by elemental analysis, conductometry, magnetic susceptibility, UV-visible, FT-IR, ¹H-NMR, X-ray diffraction, thermal analysis study, and screened for antimicrobial activity. The FT-IR spectral data suggest that the ligand behaves as a dibasic tetradeutate ligand with ONNO donor atoms sequence towards central metal ion. From the microanalytical data, the stoichiometry of the complexes has been found to be 1:1 (metal: ligand). The physico-chemical data suggests the distorted octahedral geometry for La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) complexes. The X-ray diffraction data suggests monoclinic crystal system for La(III) and Ce(III) and orthorombic crystal system for Pr(III) and Nd(III) complexes. Thermal behavior (TG/DTA) of the complexes was studied and kinetic parameters were determined by Horowitz-Metzger and Coats-Redfern methods. The ligand and its metal complexes were screened for antibacterial activity against Staphylococcus aureus, Escherichia coli, Bacillus Sp. and fungicidal activity against Aspergillus Niger, Trichoderma and Fusarium oxysporum (Fig.1.14).
Sengupta et al. [174] reported La(III) and Pr(III) complexes with macrocyclic ligands containing pendant functional groups. The free Schiff base macrocycles containing pendant groups have been synthesized by the condensation reactions of N,N-diphenylsuccinamide/adipamide, N,N dipyridylsuccinamide/adipamide with ethylenediamine. The reactions of these ligands with Lanthanum(III)/Praseodymium(III) chlorides have been carried out in ethanol and macrocyclic complexes of type [LnCl₃(mac)] have been isolated. Tentative structures of the complexes have been proposed on the basis of elemental analyses, electrical conductance, magnetic moment and spectral (IR, electronic, ¹H NMR) data. The metal ions have seven-coordinated geometry (Fig.1.15).

Brianese et al. [175] reported preparation, properties and X-ray structure of a new La(III) trichloride complex with an asymmetric compartmental cyclic Schiff base. The La(III) complex [La(H₂Lₐ)(Cl)₃] has been prepared by reaction of the preformed ligand H₂Lₐ with LaCl₃P₇H₂O or by template procedure. H₂Lₐ is the asymmetric [1+1] compartmental macrocycle containing an N₃O₂ Schiff base and an
O$_2$O$_4$ crown-like site derived by the condensation of 3,39-(3,6-dioxaoctane-1,8-diyldioxy) bis (2-hydroxy benzaldehyde) and 1,5-diamino-3-aza methylpentane. The X-ray structure of [La(H$_2$L$_A$)(Cl)$_3$] shows that the lanthanum ion fills the O$_2$O$_4$ site and is nine coordinated with a tricapped trigonal prismatic environment, the coordination sphere about the central metal ion is completed by three chloride anions (Fig.1.16).

Fig.1.16

Jerzy Lisowski and Jaroslaw Mazurek [176] reported chiral macrocyclic La(III), Ce(III), Pr(III) and Eu(III) complexes with chloride anions. The new enantiopure macrocyclic complexes [LnL]Cl$_3$.nH$_2$O or their racemic mixtures [LnracL]Cl$_3$.nH$_2$O (Ln= La$^{3+}$, Ce$^{3+}$, Pr$^{3+}$ and Eu$^{3+}$) have been synthesised in a template condensation of trans-1,2-diaminocyclohexane and 2,6-diformylpyridine. The complexes have been studied by $^1$H and $^{13}$C NMR spectroscopy. The signal assignment was based on the COSY, NOESY and HMQC measurements. The X-ray crystal structure of [LaracL]Cl$_3$ complex has been determined. The lanthanum ion in this complex is coordinated by six nitrogen atoms of the macrocyclic ligand and three chloride anions. The macrocycle exhibits a twistbent conformation of approximate C$_2$ symmetry. On the other hand, NMR spectra of the investigated compounds in methanol-chloroform solution indicate effective D$_2$-symmetry that results from the fast dynamic exchange of chloride anions (Fig. 1.17).
Benetollo et al. [177] reported Ln(III) complexes of six-nitrogen-donor macrocyclic ligands with benzyl-type peripheral substituent’s, and crystal structure of [La(NO$_3$)$_2$(H$_2$O)(C$_{36}$H$_{38}$N$_6$)](NO$_3$)(H$_2$O). Ln(III) complexes of six-nitrogen-donor macrocyclic ligands carrying a benzyl-type group, —CH$_2$— C$_6$H$_4$—X (X= -H, -OH, or -NH$_2$), at each diimine side chain were synthesized by the metal-templated, cyclic Schiff-base condensation of 2,6-diacetylpyridine with substituted S- or R,S-1,2-diaminopropanes. The complexes were obtained as mixtures of constitutional isomers and stereoisomers, which were identified by $^1$H NMR spectra and separated by fractional crystallization. The molecular structure of the 11-coordinate complex [La(NO$_3$)$_2$(H$_2$O)(C$_{36}$H$_{38}$N$_6$)](NO$_3$)(H$_2$O) was established by X-ray crystallography (Fig.1.18).

Benetollo et al. [178] reported constitutional isomers and stereoisomers of La(III) complexes of the dimethyl substituted six nitrogen donor ligand C$_{13}$H$_{29}$N$_5$ and crystal structure of [La (C$_{13}$H$_{29}$N$_5$)(NCS)$_3$(H$_2$O)] 0.5H$_2$O complexes of La(III) with the macrocyclic ligand C$_{13}$H$_{29}$N$_5$ in which each diimine side chain carries a -CH$_3$ substituent, were synthesized by the metal-templated cyclic Schiff-base condensation.
of 2-6 diacetylpyridine with (R), (S) and (R,S) 1,2 diaminopropane. The complexes were obtained as mixtures of constitutional isomers and stereoisomers, which were identified by \(^1\)H NMR spectra and separated by fractional crystallization. The molecular structure of the 10 coordinate complex \([\text{La}(\text{C}_{13}\text{H}_{29}\text{N}_{5})(\text{NCS})_3(\text{H}_2\text{O})]\) 0.5\(\text{H}_2\text{O}\) was established by X-ray crystallography.

Patil et al. [179] reported biological activity of 22-membered N\(_4\) tetraaza macrocyclic triazoles and their metal complexes. A series of La(III) and Th(IV) complexes have been synthesized by template condensation of ortho-phthalaldehyde, bis-(4-amino-5-mercapto-1,2,4-triazole-3-yl)alkanes and La(NO\(_3\))\(_3\) .6\(\text{H}_2\text{O}\)/ Th(NO\(_3\))\(_4\) .5\(\text{H}_2\text{O}\) in ethanol. These complexes were characterized by elemental analyses, magnetic susceptibility, molar conductance, spectral (IR, UV-Vis, \(^1\)H NMR FAB-mass), and thermal studies. Elemental analyses suggest 1:1 stoichiometry. Spectroscopic study indicates that the coordination occurs through nitrogen of azomethine group and bridging bidentate nitrates. All the Schiff bases and their La (III) and Th (IV) complexes have been screened for their antibacterial (Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa) and antifungal activities (Aspergillus niger, Aspergillus flavus and Cladosporium) by the minimum inhibitory concentration method. The DNA cleavage study was done by Agarose gel electrophoresis (Fig.1.19).

![Diagram](image)

**Fig.1.19**

Ilhan et al. [180] reported synthesis, structural characterization and electrochemical studies of new macrocyclic Schiff base containing pyridine head and its metal complexes. Then La(III) complexes were synthesized by the template effect by the reaction of 2,6-diaminopyridine and 1,2-bis(2-carboxyaldehyde phenoxy)ethane and La(NO\(_3\))\(_3\).\(\text{H}_2\text{O}\), respectively. The ligand and its metal complexe
have been characterized by elemental analysis, IR, $^1$H and $^{13}$C NMR, UV–Vis spectra, magnetic susceptibility, gravimetric thermal analysis, conductivity measurements, mass spectra, and cyclic voltammetry (Fig.1.20).

![Fig. 1.20](image)

Ilhan et al.[181] studied the synthesis and spectral studies of macrocyclic Pb(II), Zn(II), Cd(II) and La(III) complexes derived from 1,4-bis(3-aminopropoxy)butane with metal nitrate and salicylaldehyde derivatives. Eight new macrocyclic complexes were synthesized by template reaction of 1,4-bis(3-aminopropoxy)butane with metal nitrate and 1,3-bis(2-formylphenyl)propane or 1,4-bis(2-formylphenyl)butane and their structures were proposed on the basis of elemental analysis, FT-IR, UV–Vis, molar conductivity measurements, $^1$H NMR and mass spectra. The configurations of La(III) and Pb(II) were proposed to probably octahedral and Zn(II) and Cd(II) complexes were proposed to probably tetrahedral (Fig.1.21).

![Fig.1.21](image)
1.5 Aim of the present investigation:-

In view of above mentioned facts, it was planned to synthesize macrocyclic ligand and their metal complexes followed by structural investigation using spectroscopic and diffraction techniques along with biological activity.

The present study deals with the synthesis of macrocyclic ligands derived from substituted diketones and ethylene diamine and their metal complexes of La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) ions.

The following substituted diketones are used for synthesis of macrocyclic ligands.

1) 1-(4-chloro-2-hydroxyphenyl)-3-phenylpropane-1,3-dione.
2) 1-(4-chloro-2-hydroxyphenyl)-3-p-tolylpropane-1,3-dione.
3) 1-(4-chloro-2-hydroxyphenyl)-3-(4-methoxyphenyl) propane-1,3-dione.
4) 1-(4-chloro-2-hydroxyphenyl)-3-(4-chlorophenyl) propane-1,3-dione.
5) 1-(4-chloro-2-hydroxyphenyl)-3-(4-nitrophenyl) propane-1,3-dione.

The characterization of macrocyclic ligands have been carried out by elemental analysis, $^1$HNMR, FT-IR and electronic absorption spectra. The complexes are characterized by elemental analysis, electron absorption spectra, conductometry, thermal analysis, IR spectroscopy and powder X-ray diffraction techniques.

The general structure of the metal complexes synthesized in the present study is shown in Fig 1.22.

![Fig.1.22](image-url)
1.6 References:-


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