

## APPLICATIONS OF TRANSITION METAL MACROCYCLIC COMPLEXES

M. C. R. Peiris

*Board of Study in Chemical Sciences*

Applications of the transition metal macrocyclic complexes (TMMC) can be divided into several sections such as antibacterial drugs, catalysts, MRI scanning agents, antioxidants, ion transporters, radiopharmaceuticals etc, according to the way they use. Among these applications catalytic activity of these macrocyclic complexes has a major contribution to the green chemistry. Most of the TMMC are synthesized to act as the catalyst for various reasons, due to their high thermal stability, unusual structural, electronic and electrochemical properties. Some natural macrocyclic complexes have shown the capability of using as catalysts for many transformations such as vitamin B<sub>12</sub>. Catalysis can be divided into a number of areas, depending on the substrate and the catalytic reaction. One of the prime areas of the initial effort in catalysis [1] has been the small molecule activation, such as O<sub>2</sub>, NO<sub>2</sub>, NO, H<sub>2</sub>S and CO<sub>2</sub>.

Transition metals such as Cu, Ni, V, and Fe also act as catalysts themselves, but these metal catalysts have several drawbacks. These metals show the catalytic activity only when it is in 100% pure form, but the pure metals such as Pt are highly expensive. Another thing is, in higher potentials these metals can undergo oxidations that changes their surface properties. Dust, moisture, higher and lower temperatures will directly influence the catalytic activity of the metal. Many of these drawbacks can be eliminated by using these metals in the macrocyclic form. The common transition metals used in macrocyclic catalysts are Fe, Co, Ni, and Cu, and the macrocyclic ligands include chelating atoms N<sub>4</sub>, N<sub>2</sub>O<sub>2</sub>, N<sub>2</sub>S<sub>2</sub>, O<sub>4</sub>, and S<sub>4</sub>. This can be further explained by considering the interaction between small molecules and a transition metal. Electron transition occurs first from small molecules such as oxygen and carbon dioxide into the empty  $d_z^2$  orbital, forming a  $\pi$  bond, lowering the anti-bonding  $\pi$  orbital's and raising the energy of the  $d_{xz}$  and  $d_{yz}$  orbitals of the transition metals. This allows the electron transition from these filled orbital's to the anti-bonding  $\pi$  orbital, and resulting in catalytic activity.

These TMMC are also very popular in the medicinal field [2, 3] due to their resistivity towards the gram (-) and gram (+) bacteria [2], fungal growth and as the virus inhibitors. Few of the drugs such as VL-1, CoL-2, NiL-3 (Fig.1.) shows the inhibitor activity towards the microbial growth.

A number of macrocyclic chelators have been proposed as MRI contrast agents or as bifunctional agents for labeling antibodies and peptides with several radionuclides. Most frequently used paramagnetic metal in MRI contrast agent is Gadolinium [Gd (III)] ion, but free Gd (III) radionuclide are extremely toxic. Therefore it is required as they are administered to patients as chelates. When the metal ion is complexed, they become thermodynamically stable and kinetically inert (Fig. 2.).

Radiopharmaceuticals [4] are also emergent drugs in tumor therapy; new therapeutic radiopharmaceuticals have been recently prepared aiming to deliver large radiation doses to the diseased sites while sparing normal cells. For this macrocyclic complexes are used as the transporter of the radiopharmaceuticals.

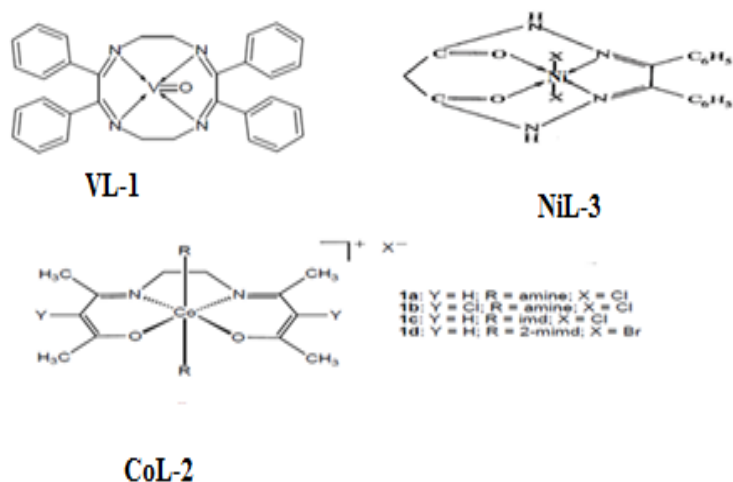


Figure 1: Antimicrobial drugs consist of transition metal atoms in the macrocycle. **VL-1**, shows antibacterial activities against *E.coli*(-), *S.aureus*(+) *M.luteus*(+) and *B.licheniformis* (+). **CoL-2**, Class of drugs was performed using model infected with Herpes Simplex Virus Type 1 (HSV-1) and all these complexes inhibited HSV-1. **NiL-3**, Shows a very good antifungal activity towards *Aspergillus flavus* and *A. niger*.

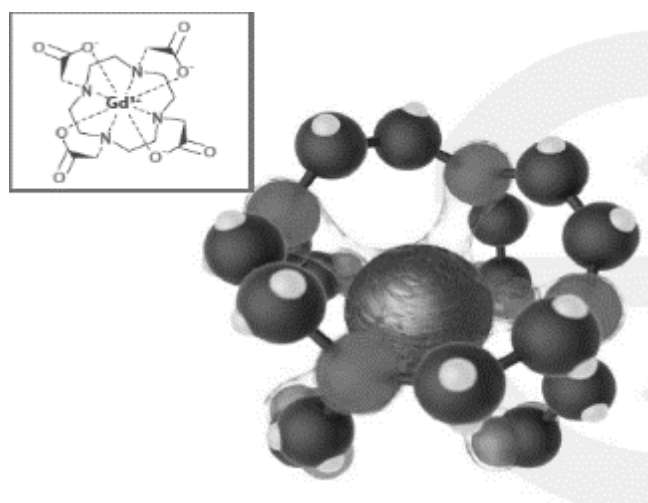


Figure 2: Metal complexes which are using for cell labeling and magnetic resonance imaging applications.

Macrocyclic complexes also act as ion transporters [5], especially cation transporters and those were one of the early focal points in macrocyclic chemistry, revolving primarily around the crown ethers and cryptands. Later efforts have been to provide switches to control the rates of cation transport. Further the transport capabilities of synthetic macrocycles is also used in analytical chemistry. Because of their selective complexation of a variety of cations, the crown ethers and related macrocycles have been widely used for separations and analyses. While transport efforts have largely involved metal cations, more recent developments have led to the use of macrocycles for transport of more complex molecules such as nucleosides. Not only these applications, macrocyclic complexes have many other applications too, such as antioxidant activity.

**References**

1. Delgado, R., Costa, J., Krassimira, P., Luís, G., Lima, M.P., Lanthanide complexes of macrocyclic derivatives, *Pure Appl. Chem.* 2005, 77 (3), 569–579.
2. Panchbha, M. A., Paliwal, L. J. and Bhavi, N S., “Synthesis and characterization of complex compounds of Tetraza-aza Macrocyclic ligands”, *J. Chem.* 2008, 5(SI) 1048-1054.
3. Sharma, R., Singh, R., Pawar, S. and Chauhan, A., “Studies of transition metal complexes and Their antibacterial activities” , *J. Amer. Chem. Soc.* 2010, 6 (9).
4. Zheng, Q., Dai, H., Matthew, E. M., Malloy, C., Pan, C.Y. and Hong Li, W\*., New Class of Macrocyclic Lanthanide Complexes for CellLabeling and Magnetic Resonance Imaging Applications, *J. Amer. Chem. Soc.* 2005, 9 (46).
5. Almy, J., Garwood, D. C. and Cram, D. J., *J. Amer. Chem. Soc.* 1973, 95, 2961.