

A SHORT REVIEW ON BIOLOGICAL APPLICATIONS OF MACROCYCLIC COMPLEXES OF CHROMIUM

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ABSTRACT

The main intent of the article is to lay out a brief valuation of biological significance of latest macrocyclic complexes of chromium metal with highlighting the synthesis of these complexes and their applications as antimicrobial agents. Antibiotic ministrations are the leading perspective of current medical science which is used to resist infections. But nowadays, power of established drugs against microorganisms is persistently decreased due to bacterial resistivity, which creates a serious issue related to public health. Extensive work has been disclosed on macrocyclic complexes of first row transition metals performing as remedy for copious microbial infections and these reports express their equal or higher capacities to resist the infection as compared to other clinically useable drugs. So here in this review, the synthesized complexes of chromium metal, their precursors and their reported biological activities have been discussed.

Keywords: Antimicrobial Activity, Chromium, Macrocyclic Complex.

INTRODUCTION

Researchers are mainly focusing on the synthesis of new complexes having their utility in various fields like industrial, analytical, optics, electronics, solar energy, catalytically, dyes, pharmacological, biomedical, hydrometallurgical extraction *etc* [1-8]. In coordination chemistry, the macrocyclic complex forming chemistry sub-branch acquired considerable more attention over the last few years because of their prospective applications in copious fields. They can willingly construct stable complexes by forming a ring with a variety of metal ions [9-20]. So this branch is becoming a major growing area of exploration as natural occurring and synthetic both macrocyclic complexes proceeding their extensive roles for discovery of new drugs, nanotechnology, act as receptors (for both anion and cation), therapeutics and identification of molecules *etc* [21-27]. In several biological processes, metal ions play a key role for treatment of diseases by combining components with the biological system. Lots of naturally occurring complexes (Hb, chlorophylls, vitamin B12 *etc*) have been revealed having various metals as central atom and playing significant role in copious biological processes [28-53]. Human beings and animals get microbial infections, prompting the uses of antibiotics and antibiotic resistance occurred by the frequently uses of it. A major global threat to mammalians and environmental health is caused by antimicrobial resistance due to microbial dispersive property, their existence in the air and their ability to subset of the population to survive exposure to bactericidal drugs concentration [54]. That results the higher medical costs, stay in hospitals for longer time and enlarged transience. There are several microbial pathways against pathogens to balance the antibacterial resistance. Replacement of clinically organic fabricated drug by the metal fabricated drugs is one of them. These metal based medicines have expertise to change the configuration, numbers, shape and oxidation number of complexes, which leads the replacement of organic fabricated drug by them. In metal based complexes by the ring formation the contrariety of central atom gets reduced to markedly due to the partial charge separation and that's increases stability of complexes by the non-localized π -electrons that spread over the whole cyclic ring. As the result of this process, lipid loving nature of complex increases and that permits the complex to enter in the cell membrane of microorganisms. Here in microbial cell, these complexes also disturb the respiratory system of it and blocks the synthesis of DNA-proteins, which retard the further division of the organism. Cr is very adaptable M and it can form copious species with variable oxidation numbers from (-IV) to (+VI). Complexes with (0), (+III), and (+VI) oxidation states of chromium are frequently found and utilized in ambient conditions [55]. Out of all the metals it has been reported to interact with various amino acids like cysteine and histidine of microbial cellular proteins, and form stable complexes. According to the reports it is recommended that for adequate daily dietary intake of chromium 35 μg for men and 25 μg for women is essential as it plays a key role in proper functioning of brain and heart, for blood sugar regulation, and to breakdown the lipids and sugars. In biotransformation it retards the variation in DNA replication loyalty and expands mutation frequency. In this review article, we listed latest macrocyclic complexes containing chromium as a central metal

ion, their precursors, structure of the synthesized complex and shown antimicrobial activities by them. It will help researchers to understand how the geometry of any complex can change its action [56].

SYNTHESIS OF THE MACROCYCLIC COMPLEXES OF CHROMIUM

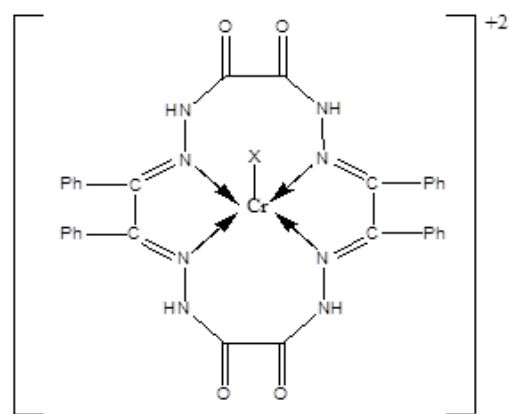
Materials: By studying all these reported paper in this review it can be concluded that all chemicals were taken of analytical grade reagents with high purity for the synthesis purpose, metal salts were bought of Merck, Ranbaxy and used as received.

Process of synthesis of macrocyclic complexes:

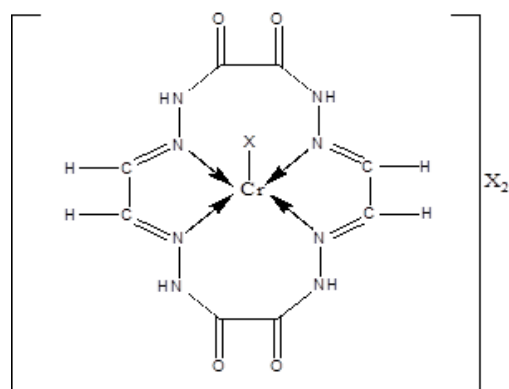
There are several methods like conventional, microwave or template by which we can synthesize complexes by condensing both typed precursors in presence of metal ion as central atom ion. Methanolic or ethanolic solutions of both the ligand precursors were added in round bottom flask followed by metal salt in 2:2:1 or 1:1:1 molar ratios. The reaction solutions were stirred continuously on magnetic stirrer and refluxed for about 6-8 hours. The color change of the newly synthesized complexes was noticed. The round bottom flask was kept aside for its cooling. For filtration and washing of these complexes methanol or ethanol solvents were used and dried in vacuum. These complexes were taken for their studies. Copious biological activities namely antibacterial, antifungal, anti-inflammatory, anti-cancer, nematocidal, pesticidal, antioxidant *etc* of these complexes was also explored. Reports indicated that almost all the tested complexes possess antimicrobial actions against variable antibacterial and antifungal strains [57].

EXTENSIVE LITERATURE SURVEY

Enormous work has been done on macrocyclic complexes of transition metals. Here in this article, we collected latest macrocyclic complexes containing Cr as central metal ion. Oxalylidihydrazide and Diphenyl-ethanedione formed complex (1) by the condensation reaction having chromium metal ion as template. A square pyramidal geometry with five coordination number have been proposed by considering various studies namely NMR, electronic, IR, FAR-IR, molar conductance measurements, magnetic susceptibility and elemental analyses. Obstructing capacities of these complexes were demonstrated against various infectious bacteria namely *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* & *salmonella typhi*. Results showed that the complexes exhibit outstanding activities. Excluding acetate and nitrate, chloride complexes of chromium having formulae $[\text{Cr}(\text{C}_{32}\text{H}_{24}\text{N}_8\text{O}_4)\text{Cl}]\text{Cl}_2$ presented minimum inhibiting concentration similar to the standard drug Linezolid's minimum inhibiting concentration against bacterial strain *Staphylococcus aureus* and also registered minimum inhibiting concentration against *salmonella typhi* as shown by standard antibiotic Linezolid [58].



(1)

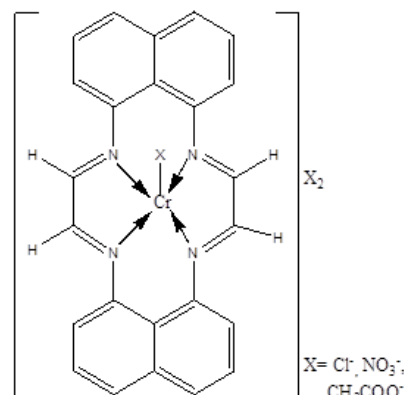


(2)

A series of chromium centred macrocyclic complexes having formulae $[\text{Cr}(\text{C}_8\text{H}_8\text{N}_8\text{O}_4)\text{X}]\text{X}_2$ (2); {where X may be Cl^- , NO_3^- or CH_3COO^- } produced by condensing oxalylidenediamine and ethane-dial using chromium metal salt as templates in methanol solvent. A number of studies namely UV/Vis, IR, FARIR, magnetic susceptibility etc supported a square pyramidal geometry of these complexes with coordination numbers five. All the reported complexes were biologically screened *ex vivo* against a variety of infectious bacteria *viz.* *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* & *salmonella typhi*, via spot-on-lawn on Muller Hinton Agar method and results showed that these complexes exhibit amazing activities. Except chloride complexes, nitrate and acetate both complexes showed minimum inhibiting concentration against *salmonella typhi* and *Escherichia coli* respectively, which is equivalent to standard drug Linezolid's minimum inhibiting concentration against these same bacterial strains. The components namely $\{>\text{C}=\text{N}-\text{R}\}$ linkage and presence of heteroaromatic nuclei in such complexes increases biological activities by increasing hydrophobic characters and liposolubility of the complex that leads the penetration of that compound into the microbial cell membrane and uplifting of microbial activities are shown by the complexes in presence of these kind portions [59].

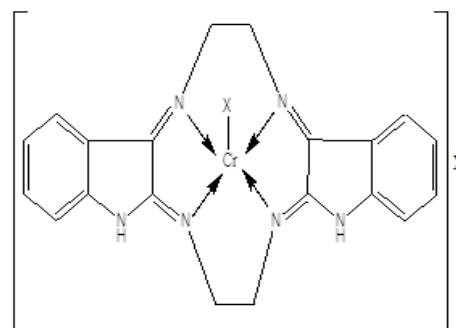
Condensation reaction between naphthalene 1,8-diamine and glyoxal in methanol solvent using chromium metal salts (Cl^- , NO_3^- or CH_3COO^-) as metal templates formed a complex having formulae $[\text{Cr}(\text{C}_{24}\text{H}_{16}\text{N}_4)\text{X}]\text{X}_2$. Based on several studies *viz.* Mass spectrometry, NMR, IR, etc, a square pyramidal geometry with coordination number five have been reported. Proposed structure of the complexes represented in figure (3). *Ex vivo* antimicrobial screening of all synthesized complexes were explored versus four bacterial strains namely *Escherichia coli*, *Bacillus subtilis*, *Bacillus stearothermophilus* & *Pseudomonas putida* and two fungal strains namely *Aspergillus flavus* & *Aspergillus niger*. Antibacterial activity results were contrasted with standard drugs namely Chloramphenicol and Streptomycin and antifungal activities were compared with Cyclohexamide popular drug. All complexes showed antibacterial activities against all bacterial strains but their obstructing capacities were greater against gram negative bacteria than the gram-positive bacteria. $[\text{Cr}(\text{C}_{24}\text{H}_{16}\text{N}_4)(\text{NO}_3)](\text{NO}_3)_2$ complex exhibited more inhibiting

potential as compare to the other complexes against both fungal strains and author suggested that except chelation there may be several factors that can influence the antimicrobial activities of these complexes like dipole moment of the complex, dissolving power in the solvent and change in conductance by addition of metal ion etc [60].



(3)

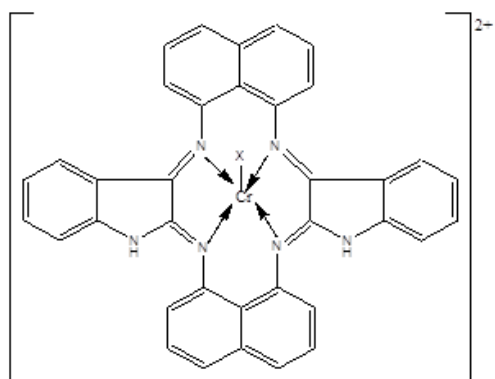
X = Cl^- , NO_3^- ,
 CH_3COO^-



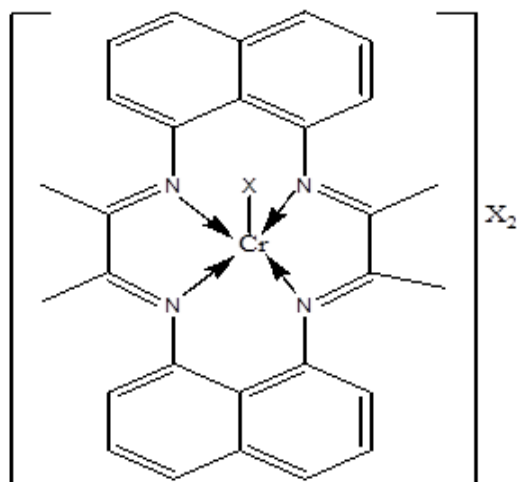
(4)

A series of chromium complexes having formulae $[\text{Cr}(\text{TML})\text{X}]\text{X}_2$ (4); {where X may be Cl^- , NO_3^- or Ac^- } was obtained, *via* both conventional and microwave methods by condensation reaction of tribulin (1H-Indole-2,3-dione) and 1,2-Diaminoethane. By considering various physico-chemical analysis techniques *viz.* analyses of elements, measurement of conductance, magnetic susceptibility measurement, IR, FARIR, UV/Vis spectral studies *etc.* a square pyramidal geometry having five coordination numbers were proposed for these synthesized complexes. Spot on lawn on miller Hinton agar method was adopted for *ex vivo* antibacterial screening of these complexes and were performed against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* and *salmonella typhi* bacterial strains and results indicated that all complexes showed minimum inhibiting concentration greater than the standard antibiotics *viz.* Linezolid and Cefactor. Formation of a ring around the metal increases the penetration power of the complex into the microbial cell membrane, which may lead the activity of the complexes [61].

A novel series of complexes having formulae $[\text{Cr}(\text{C}_{36}\text{H}_{22}\text{N}_6)\text{X}]\text{X}_2$ (5); {where X may be Cl^- , NO_3^- or Ac^- } manufactured by Singh et al by the cyclo-condensation reaction of naphthalene-1,8-diamine and 2,3-Indolinedione having Chromium (III) metal ion as central moiety in methanol solvent. Various physico-chemical analysis techniques namely elemental analyses, conductance, UV/Vis, IR, mass spectrometry *etc.* favored a square pyramidal geometry with coordination number five for these complexes. Agar well diffusion method and poisoned food technique were used for the *ex vivo* assessment of all these complexes against antimicrobial and antifungal strains respectively. The complexes were screened contra *Staphylococcus aureus* & *Bacillus subtilis* gram positive and *Pseudomonas aeruginosa* & *Escherichia coli* gram negative bacterial strains. *Aspergillus flavus* & *Aspergillus niger* fungal strains were chosen for antifungal assessment. For the comparison of the resulted minimum inhibiting concentrations of these complexes, standard antifungal Amphotericin-B & antibacterial Ciprofloxacin were applied. All complexes showed remarkable but in consistent results for both of the activities [62].

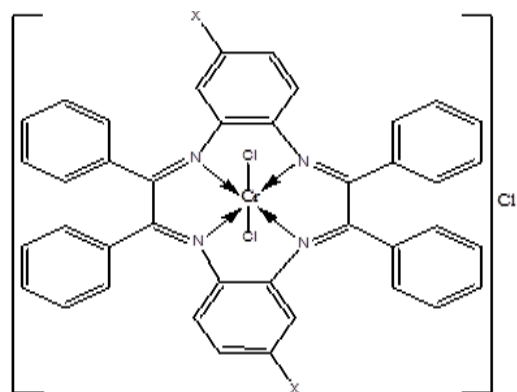


(5)



(6)

Singh *et al* synthesized a N_4 -tetradendated corresponding macrocyclic ligand ($C_{28}H_{24}N_4$) and its $[Cr(C_{28}H_{24}N_4)X]X_2$ typed complexes (6); {where X may be Cl^- , NO_3^- or Ac^- }, by reacting naphthalene-1,8-diamine with 2,3-butanedione and having chromium metal ion as central moiety in methanol solvent *via* template condensation method. A square pyramidal geometry with coordination number 5 have been proposed by considering various physic-chemical techniques such as analyses of elements, magnetic measurement, molar conductance, UV/Vis, IR spectroscopy. Both *Aspergillus niger* and *Aspergillus fumigatus* fungal strains were taken for antifungal assessment of these complexes and compared with standard antifungal drug Fluconazole. Results indicated that $[Cr(C_{28}H_{24}N_4)Cl]Cl_2$ complex showed 55.5% mycelial growth inhibition against *Aspergillus fumigatus*, which is highest over nitrate and acetate chromium complexes. Apart from chelation other aspects namely, solubility of complexes, dipole moment, and metal ion influenced conductance may be responsible for the antifungal activities of these complexes [63].



(7)

Masih *et al* [64] reported pesticidal, nematocidal, antibacterial and antifungal screening of chromium (III) macrocyclic complexes obtained by the reaction of ligands 2-[4-X-2-(2-oxo-1,2-diphenyl-ethyleneamine)-phenylamino]-1,2-diphenyl-ethanone; {where X = chloro[ML] and fluoro[ML^{II}]} with *O*-phenylenediamine, 4-chloro-1,2-benzenediamine or 4-fluoro-1,2-benzenediamine having chromium chloride as central moiety *via* template condensation method. Based on various spectral studies *viz.* IR, ESR, electronic spectroscopy, XRD methods and physico-chemical characterization techniques like analyses of elemental, magnetic moment measurement and conductance measurements, a octahedral geometry with coordination number six have been proposed for these reported complexes. *Escherichia coli* & *Bacillus subtilis* bacterial strains were used to evaluate antimicrobial activities of these complexes and compared with standard drug Streptomycin by using paper-disc plate method. Data's showed that $[Cr(C_{40}H_{27}N_4Cl_3)]Cl$ and $[Cr(C_{40}H_{26}N_4Cl_4)]Cl$ complexes exhibited 30 $\mu g/ml$ minimum inhibition concentrations for both bacterial strains. Against *Fusarium oxysporum* & *Rhizopus nigricans* fungal strains antifungal activity of these complexes were assessed by adopting agar-plate technique. Bavistin standard antifungal drug was used for comparison. Against *Fusarium oxysporum* fungal strain both $[Cr(C_{40}H_{27}N_4Cl_3)]Cl$ and $[Cr(C_{40}H_{26}N_4Cl_4)]Cl$ complexes showed minimum inhibition concentrations at 5.125 $\mu g/ml$.

Nematicidal activity of these complexes were performed by step by step procedure against meloidogyne incognita and results showed that as compare to ligand, complexes are more active to inhibit the egg's hatching. By the help of following equation nematicidal properties have been computed; where nematicidal property is denoted by NP, HC representing the controlled amount of hatching and hatching amount in the test plate represented by HT.

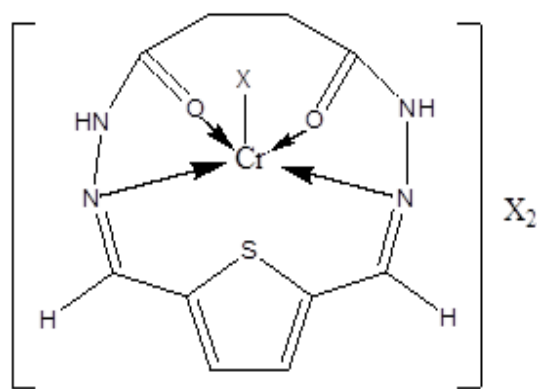
$$NP \% = (HT \times 100) \div HC$$

Pesticidal activity of these complexes was performed against Corcyra Cephalonica's fifth instar larvae and report indicated that both ligands and complexes inhibited further growth and development of that larvae. Out of all complexes $[Cr(C_{40}H_{26}N_4Cl_4)]Cl$ complex exhibited highest pesticidal activity with Lethal Concentration₅₀ = 165 mgL^{-1} against Corcyra cephalonica and were explained on the basis of inhibition of melting hormones of the Larva by that complex. Following formulae known as Abbott's formulae was used to correct Control mortality;

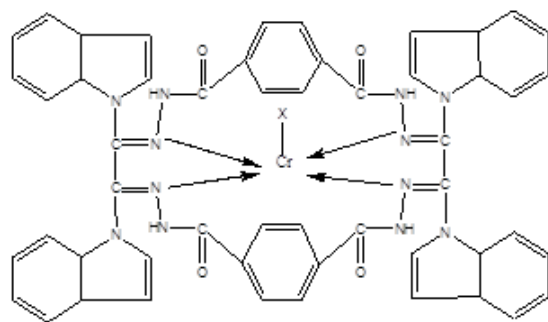
$$\begin{aligned} \text{corrected mortality}\% \\ = (\% \text{mortality observed} - \% \text{mortality in control} \\ \div 100 - \% \text{mortality in control}) \times 100 \end{aligned}$$

$[CrLX]X_2$ typed complex {where L = $(C_{10}H_{10}N_4O_2S)$, & X is Cl^- , NO_3^- or Ac^- } consolidated by the cyclocondensation reaction of butanedihydrazide and 2,5-diformylthiophene using trivalent chromium metal salt as template. Characterization of these complexes were accomplished by UV/Vis, analyses of elements, IR, ESR, FAR-IR, magnetic susceptibility measurement, powder XRD analysis, Mass spectral studies, and molar conductance measurements techniques. Based on these mentioned studies a square pyramidal geometry with 5 coordination number has been proposed for the complexes.

Powder XRD helped to prove that the reported complex had *p*bravais lattice contained triclinic crystal system. These thiophene based macrocyclic complexes were explored for *ex vivo* biological screening namely antibacterial, antifungal and antioxidant activity. Antimicrobial studies of the reported metal complex were examined *ex vivo* against *Bacillus subtilis* & *Escherichia coli* bacterial strains and *Saccharomyces cerevisiae* & *Candida albicans* fungal strains. Nitrate complex of $[Cr(C_{10}H_{10}N_4O_2S)]^{3+}$ showed excellent antioxidant activity ($IC_{50} < 50 \mu g/ml$) than the other complexes that can be explained by increased acidity of the complexes in the presence of EWG. Due to electron withdrawing groups like NO_3^- , CN^- electron affinity towards the metal centre increases in the complexes and with increasing the electron affinity efficiency to free the acidic hydrogen from the complex will also be increased. Cr has $3d^3$ electrons configuration in (+III) oxidation state and have greater affinity for completion of its $3d^5$ configuration. Higher antioxidant capacity of nitrate complex as compare to chloride and acetate was explained on the basis of above-mentioned EW nature of NO_3^- group that increases acidic nature of azomethine hydrogen [65].



(8)



(9)

Kumar *et al* [66] consolidated a series of 24-membered macrocyclic complex having formulae $[\text{Cr}(\text{C}_{52}\text{H}_{36}\text{N}_{12}\text{O}_4)\text{X}]_2$. 1,4-dicarbonyl phenyl dihydrazide and 1,2-di(indol-1-yl)ethane-1,2-dione both ligand precursors consolidated the ligand ($\text{C}_{52}\text{H}_{36}\text{N}_{12}\text{O}_4$) by the condensation reaction. Analyses of element, molar conductance measurement, and magnetic susceptibility measurements were used for physico-chemical characterization of the ligand and its complexes. Various spectral techniques namely IR, ^1H NMR, gas chromatography mass spectrometry, and UV/Vis spectroscopy supported a square pyramidal geometry of that complex with five coordination number. *Escherichia coli* & *Pseudomonas aeruginosa* (gram negative) and *Bacillus subtilis* & *Staphylococcus aureus* (gram positive) bacterial strains were chosen for antibacterial assessment. Results indicated that these complexes expressed antibacterial activities against *Escherichia coli* and *Bacillus subtilis*. Antifungal activity was explored against two yeasts (*Candida albicans* and *S. cerevisiae*) and it was found that all complexes expressed antifungal activity. The increased activity of the complexes were explained by Tweedle's chelation theory and overtones cell permeation that stated, that ring chelation decreases the metal ion polarity by partial charge sharing and π -electron delocalization in the whole ring. Due to this lipophilicity of the complex increased and penetration power of that complex into the microbial cell also increases that retard further growth of microbes.

For antioxidant activity exploration DPPH (Diphenyl picrylhydrazyl) method was adopted and % free radical scavenging activity of the complexes was calculated by the following formulae:

$$\% \text{ Radical scavenging activity} = [(A_0 - A_c) / A_0] \times 100$$

Where A_0 = absorbance of the control & A_c = sample's absorbance at C concentration.

Reports indicated that with changing concentration of complexes antioxidant activity varies and all complexes performed moderate to significant activity.

The disk diffusion agar method was adopted for interpreting antimicrobial activities of these complexes and the free ligand. Gram positive *Staphylococcus aureus* & *Bacillus subtilis* and gram negative *Pseudomonas aeruginosa* & *Escherichia coli* bacterial strains were taken for the biological assessment of these complexes and Imipenem drug were used for comparison. Results were indicated vaster toxicity of the complexes towards gram positive strains as compare to gram negative

strains and reason for above changeable toxicity of both strains were explained by the structural dissimilarities in the cell wall's of both strains. Complexes showed greater activity than the free radical. Similarly *Penicillium species*, *Rizoctonia species*, and *Aspergillus species* yeasts were chosen for exploration of antifungal activity and compared with Miconazol standard antifungal drug. Apart from free ligand and metal ion complex, dimethylsulfoxide (control) showed negligible activity and by the observed data's it can be concluded that acetate complex of chromium $[\text{Cr}(\text{C}_{52}\text{H}_{36}\text{N}_{12}\text{O}_4)\text{OAC}](\text{OAC})_2$ showed maximum activity (~90%) against *Aspergillus species*.

Anti-inflammatory activity was studied in albino rats against carrageenin induced oedema. The paw volume inhibition for each rat was calculated by the given formula.

$$\% \text{ antiinflammation activity} = (1 - V_t/V_c) \times 100$$

Where V_t = paw volume of oedema in phenyl Butazone standard drug &

V_c = paw volume of oedema in control group

For exploration of anti-inflammatory action 25, 50 and 100 g/kg p.o these three grades dose were used of these complexes & phenylbutazone, and results indicated that these complexes showed moderate to satisfactory activity.

Rahman *et al* [67] reported the synthesis of black yellow colored N_2O_2 -tetradentate imine ligand ($\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2$) and its complexes with chromium nitrate in 1:1 molar ratios. The reaction of 1-formyl-2-naphthol with 1,2-benzenediamine in ethanolic solution formed $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2$ ligand with ejection of two water molecules and analysis of the synthesized complex and its free ligand were done by various techniques namely IR, ^1H NMR, TGA, FTIR Spectroscopy, melting point measurement, analyses of elements, molar conductance measurement, UV/Vis, and magnetic susceptibility measurements. The reported complexes were paramagnetic (existence of unpaired electrons) and showed non electrolytic nature as they did not ionize at all in solution so these are poor electricity conductors. These studies helped the author to report an octahedral geometry of the $\text{Cr}(\text{III})-(\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2)$ complex. Agar well diffusion method was applied to examine *ex vivo* antibacterial studies of ligand and its complex contra gram negative *Escherichia coli* bacterial strain and gram positive *Staphylococcus aureus* & *Bacillus subtilis* bacterial strains. Activity shown by the complexes was higher than the free ligand and was explained by the chelation theory and overtone notion. Apart from chelation, dipole moment, solubility, geometry of the complex, coordination number, size, concentration, steric factors, metal ion redox potential etc were also mentioned that influences the antibacterial activity of the complexes. For antifungal screening of ligand and its complex *Candida glabrata*, *Aspergillus niger* and *Trichophyton rubrum* three fungal strains were chosen and well diffusion method was adopted to explore the growth in Potato dextrose agar nutrient. Complexes showed greater activity than the free ligand. As DMSO (dimethylsulfoxide) is used as solvent in both biological screening so DMSO alone was also screened and it was found that it did not show any of the activity.

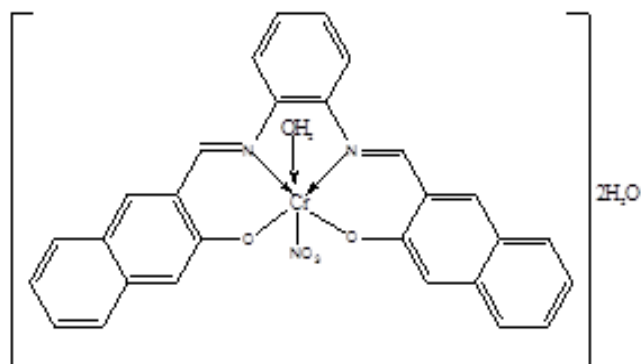
$[\text{Cr}(\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2)]$ complex showed best results to bind CT-DNA (calf thymus DNA), analyzed by titrating with electronic absorption spectroscopy method, which states that by the changing concentration of the CT-DNA the absorbance of the complex will also change in electronic absorption spectra. Results indicated that with increasing concentration of CT-DNA the absorbance for the complexes reduced due to intercalative interactions. Viscosity measurement method was adopted to explain the interaction between DNA and complex and agarose gel electrophoresis method was used to study the imine chelates-DNA binding activity.

For the treatment of malignancy (uncontrolled cell division) nowadays, so many chemical drugs are used named as cytotoxic drugs. Chemotherapy which includes; inactivation of reactive carcinogenic cell by an enzyme or chemical, prevention of formation of active species, scavenging process occurs those retard the carcinogenic cell to intact and combine with DNA, and then antioxidant and free radical scavenging, these four steps for the treatment of these carcinogenic cells. For the evaluation of cytotoxic potential of $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2$ ligand and its complex, HCT-116 cell line, HepG-2, and MGF-7 cell lines with 0-10 μm concentration range were taken. Results indicated better cytotoxic potencies of the complexes than the individual ligand and the positive reason for this activity was explained by the nature of metal ion and complexation position that

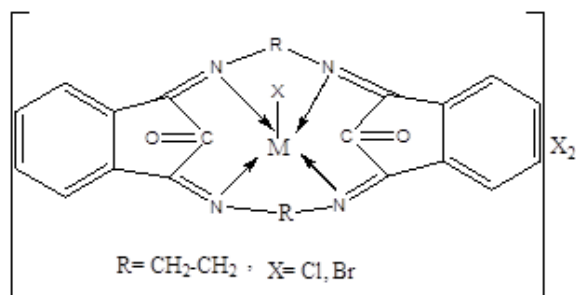
influences biological properties. $[\text{Cr}(\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2)]$ complex showed Inhibitory Concentration₅₀ value 8.2 $\mu\text{g}/\mu\text{l}$ in case of the MGF-7 cancer cell. Inhibitory concentration percentage was estimated spectro-photometrically at 564 nm wavelength with an ELISA reader by the following formulae:

$$(IC)\% = \frac{(\text{control } O.D - \text{Ligand } O.D)}{\text{control } O.D} \times 100$$

Resulted complex and ligand were also examined for their binding ability with protein- tyrosine kinase receptor as 3D- model (amino acid in TRK and ligand both are bonded through hydrogen bonding) performed *via* the receptor builder interface of the molecular operating environment program that measures the interaction of sample complex with C-kit receptor and also find out the binding free energy of these inhibitor inside the C-kit receptor. Results indicated that hydrogen bond formed between docked $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_2$ ligand and the amino acid in tyrosine kinase receptor was same as those between the ligand and amino acid.



(10)



(11)

Sharma *et al* [68] synthesized novel chromium (III) macrocyclic complexes having formulae $[\text{Cr}(\text{C}_{22}\text{H}_{16}\text{N}_4\text{O}_2)\text{X}]_2$; {where X may be Br⁻ or Cl⁻} by the cyclo-condensation of 1,2-diamineethane and 2,2-dihydroxyindane-1,3-dione having Cr(III) metal salts as templates. A square pyramidal geometry with five coordination number has been proposed for these complexes by considering various characterization methods namely magnetic susceptibility, analyses of elements, electronic spectra, molar conductance measurement, mass spectrometry, IR, and XRD methods. To find out thermal stability of these reported complexes thermo-gravimetric analysis was done in nitrogen atmosphere (temp. range 10-500°C). TGA thermograms for complexes depicted at 210-250°C & at 250-500°C stages of thermal decomposition.

Bacillus stearothermophilus & *Bacillus subtilis* gram positive and *Pseudomonas putida* & *Escherichia coli* gram negative bacterial strains were 13. H. Srour, L. P. Maux, S. Chevance, G. Simonneaux, *Coord. Chem. Rev.* **257**, 3030, (2013). (<http://dx.doi.org/10.1016/j.ccr.2013.05.010>).
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chosen to perform antibacterial screening of prepared complexes by Agar well diffusion method. (100-1ppm) variable concentration ranges were used to prepare solution in DMSO and compared the results with Streptomycin and Chloramphenicol standard drugs. Results were indicated that $[\text{Cr}(\text{C}_{22}\text{H}_{16}\text{N}_4\text{O}_2)\text{Br}]_2$ complex showed activity for gram positive *Bacillus stearothermophilus* bacteria that was coequal with standard drug's minimum inhibitory concentration. The same complex performed activity contra *Escherichia coli* that was closer to the standard antibiotic's minimum inhibitory concentration.

CONCLUSION

In this article, the biological applications of chromium metal complex have been reviewed. Nowadays, need of metal complexes having ability to be used as healing agent is steadily increasing. So here the Chromium metal complexes that can be used as medicinal compounds have been collected. These complexes showed diverse applications in pharma-chemistry namely antimicrobial, antifungal, anti-inflammatory, anti-cancer, nematocidal, pesticidal, antioxidant etc. After reading all these manuscripts it can be concluded that all the synthesized complexes were more active against microbes than their ligands. So incidentally or instantly, the summary of these complexes with their miscellaneous applications will definitely proceed their opportunities in pharma-science and material science.

ACKNOWLEDGMENTS

Authors are thankful to the Department of Chemistry, University of Rajasthan, Jaipur (India), for all kinds of support related to the work.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

THE STATEMENT OF COMPLIANCE WITH STANDARDS OF RESEARCH INVOLVING HUMANS AND ANIMALS

This review article does not contain any studies involving human participants and animals performed by any of the authors.

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