"Synthesis and Characterization of Metal Complexes of Azo Dye Ligands"

Project Submitted to Midnapore City College
for the Partial Fulfillment of the Degree of
Master of Science (Chemistry)

Submitted
By

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2023

Declaration

I do hereby declare that the present Master thesis entitled "**Synthesis and Characterization of Metal Complexes of Azo Dye Ligands"**embodies the original research work carried out by me in the Department of pure and applied Sciences, Midnapore City College, PaschimMedinipur, West Bengal, India under the supervision of Dr.Prankrishna Manna, Assistant Professor, Department of pure and applied Sciences(Chemistry), Midnapore City College,Kuturiya, Bhadutala, PaschimMedinipur, Pin-721129, West Bengal, India

No part thereof has been submitted for any degree or diploma in any University.

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Approval Sheet

This project report entitled "**Synthesis and Characterization of Metal Complexes of Azo Dye Ligands"**by Kiran Konar, is approved for the degree of M.Sc. (Chemistry).

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(Signature of Director)

(Name: Dr. Pradip Ghosh)

Date :_____

Place:_____

Acknowledgement

I would first like to acknowledge Dr. Pradip Ghosh, Hon'ble Founder Director, Midnapore City College, Paschim Medinipur for providing me the opportunity to study and complete my thesis work in this college. I am gratefully indebted to him for his very valuable comments on this thesis.

I would like to thank my thesis advisor Dr. Prankrishna Manna of the Department of Pure and Applied Sciences at Midnapore City College. The door to Dr. Manna office was always open whenever I ran into a trouble spot or had a question about my research or writing. He consistently allowed this paper to be my own work, but steered me in the right the direction whenever he thought I needed it.

I would also like to thank the other Faculties (Dr. Avishek Ghosh, Dr.Monisha Das and Dr. Jagannath Pal) and other non-teaching staffs for their support to carry out this research project. Without their passionate participation and input, the validation survey could not have been successfully conducted.

Finally, I must express my very profound gratitude to my parents for providing me with unfailing support and continuous encouragement throughout my years of study and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

Thank you

Kiran Konar

Abstract

A large number of heterocyclic azo dye substance used to impart color to textiles, paper, leather and other materials such that the coloring is not readily alteredwhen washed or expose to heat, or other factors the product will be exposed when inuse (Stothers, 2017). Popular chemical groups for azo dye production include anthraquinone, phthalocyanine and azo groups. However, azo groups are the most important chemically important and most versatile class of synthetic dyes. Azo dyes are widely used in cosmetic, pharmaceuticals, textiles, leather and food industries (Nikfar and Jaberidoost, 2014).Azo dyethat contains substituents group on the aromatic rings have also been found to be useful for non-linear optical usage while others have excellent thermal and optical properties that promotes their applications as optical recording medium, toner, inkjet printing, oil soluble light fast dyes, photoconductors for laser printers, nonlinear optics, singlet oxygen generators, dark oxidation catalysts, and high-density memory storage devices (Taura et al., 2014).

In recent years heterocyclic azo dye metal complexes attract more attention in biological application and also showing interesting co-ordination chemistry. The azo dyecontaining heterocyclic systems have been a fertile area of research for a long period,and there is a vast literature work on azo dye complexes comprising heterocyclic structures (Mallanduret al.,2017). The complexes derived from quinoline and quinoline derivatives currently attracted the interest among the azo dye ligands containing heterocyclic ring. The azo dye containing quinoline nucleus have more favored attention mainly due to their potential applications in the medicinal field (Patil et al., 2019).

The primary goal of the project is to synthesize a series of azo dye ligands of suitably positioned donor sites. Also, attempts will be made to achieve single crystals of transition metal coordination compounds (particularly that of first row metals) of synthesized azo dye ligands to determine their crystal structures with associated supramolecular features along with their spectral behavior, magnetic interactions, electrochemical properties, catalytic and biological activities, if any.

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Chapter 1: Introduction

1. Introduction

Azodye having both azo and azo-methine groups, in which azo group having outstanding donor property shows biological activities such as antibacterial, antifungal, antitumor etc,. The azo-methine group also has excellent donor property which is in coordination with transition metal ions can form stable complexes (Oforka, Mkpenie, 2007. Schiff bases and their complexes are flexible compounds synthesized from the condensation of an amino compound with carbonyl compounds and extensively used for industrial purposes and also show a broad range of biological activities including antibacterial, antifungal (Khalid Jawad Al-Adilee1 and Sarah Riyadh Hasan, 2021), antiviral, antimalarial, antiproliferative, anti-inflammatory, anticancer **(**Ikechukwu P. Ejidike, Peter A. Ajibade, 2016), anti-HIV, anthelminthic and antipyretic properties. Many Schiff base complexes show excellent catalytic activity in various reactions and in the presence of moisture. Over the past few years, there have been many reports on their applications in homogeneous and heterogeneous catalysis. The high thermal and moisture stabilities of many Schiff base complexes were useful attributes for their application as catalysts in reactions involving at high temperatures. The activity is usually increased by complexation therefore to understand the properties of both ligands and metal can lead to the synthesis of highly active compounds. The influence of certain metals on the biological activity of these compounds and their intrinsic chemical interest as multidentate ligands has prompted a considerable increase in the study of their coordination behavior. Development of a new chemotherapeutic Schiff bases and their metal complexes is now attracting the attention of medicinal chemists.

Schiff bases are an important class of compounds with a general formula such as R-HC = N-R in which R is an alkyl group that are generally synthesized by reacting as amine with aldehyde or ketones. Through passage of reaction the carbonyl carbon is changed by an imine as shown in Fig. 1 and the resulting product is called azo schiff base. The essential part in these kinds of compounds is azo-methine. These compounds have numerous applications in different fields and also used in inorganic synthesis. They have exhibited a number of biological potentials like anti-inflammatory, anti-plasmodial, antioxidant, antibacterial (TagenineJeewoth. et al, 1999), antifungal (SelwinJoseyphus, NairM. S.2008),
anticancer,(Imran Ali, et. al. 2017) and anti-depressant activities. They are also used as optical sensors in chromatographic application for sensitive and selective detection.

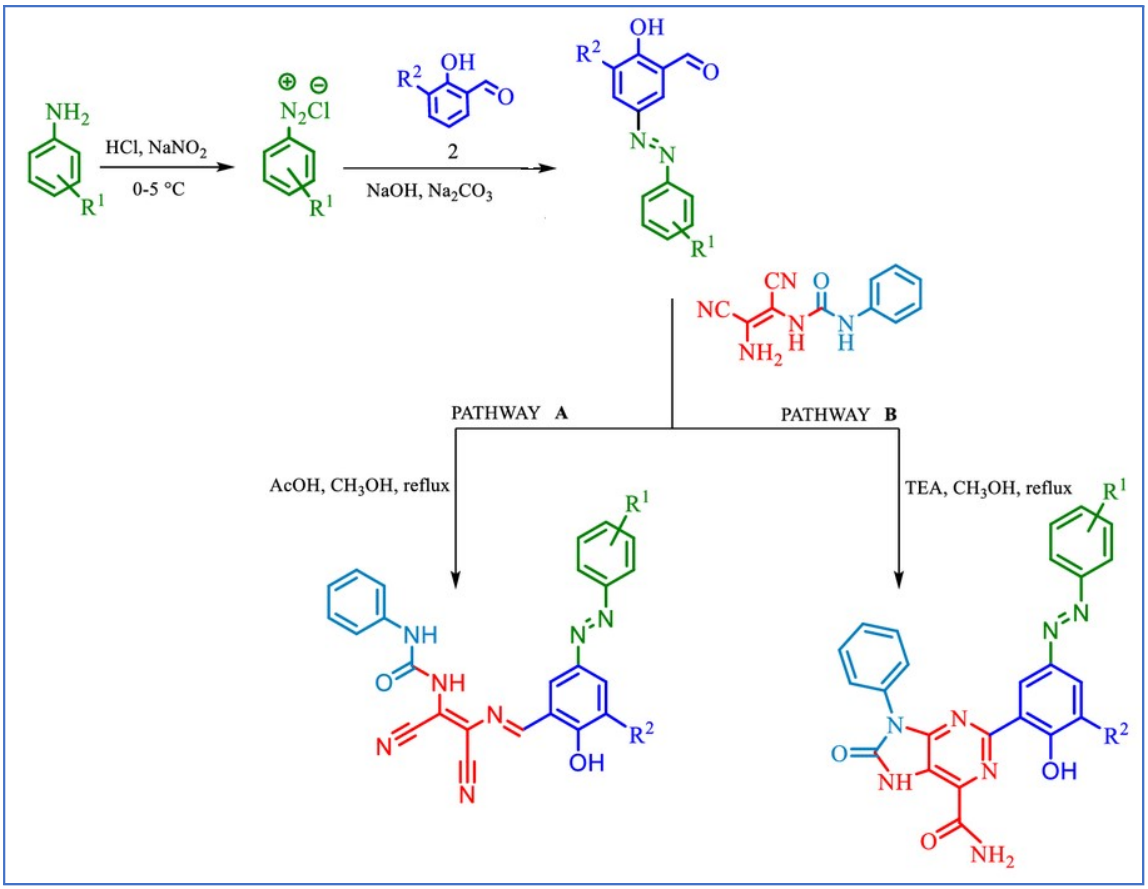


Fig1. General scheme of synthesis of azo Schiff base.

Supramolecular structures are a result of various noncovalent interactions, including van der Waals interaction, electrostatic interaction, hydrogen bonding, hydrophobic interaction, coordination, etc., some of which are often cooperatively working in one supramolecular complex.

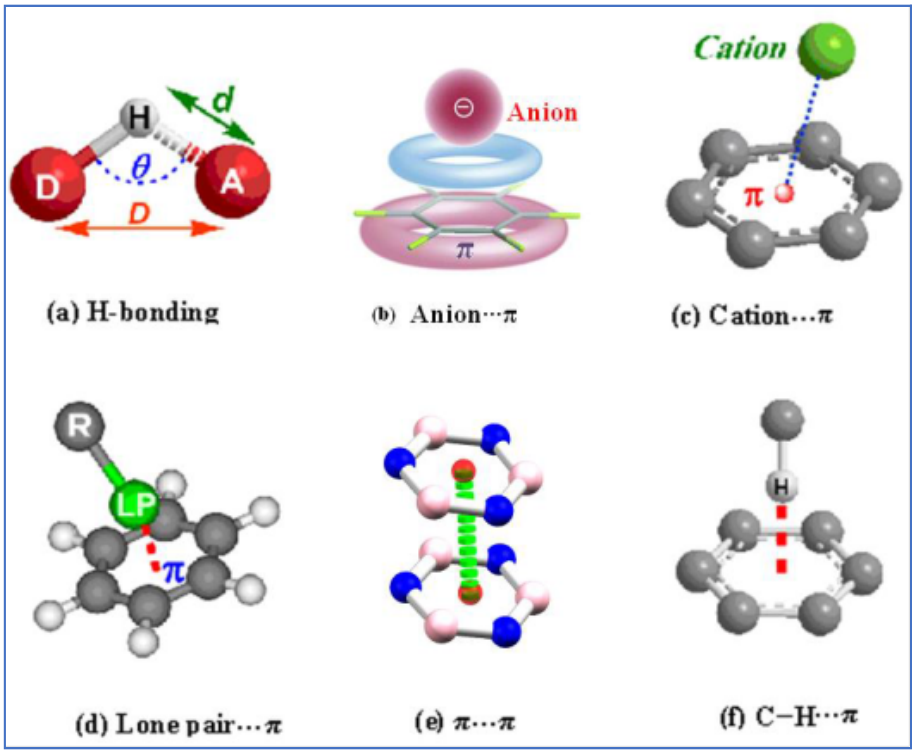


Fig 2.Various types of supramolecular interactions

Anion···π interactions: Anion-π interactions are defined as favorable non-covalent contacts between electron-rich anions and electron-deficient aromatic systems (π-acid).

Cation···π interaction: Cation···π (Jennifer C. Ma and Dennis A. Dougherty,1997) interaction is a noncovalent molecular interaction between the face of an electron-rich π system and an adjacent cation.

Lone pair···π interaction: Lone pair···π interaction is one of the most important supramolecular interactions recognized by the scientific community. supramolecular architectures based on (lone pair)···π(aryl) interactions provide stability to crystal structure.

π···π and C–H···π Interactions: Aromatic–aromatic or π–π interactions are important non-covalent intermolecular forces similar to hydrogen bonding. Although π···π interactions are accepted as weak, they have been recognized to play an important role in the folding and the thermal stability of proteins. C–H···π interaction (M.Nishio et al 1995)can also be considered as the weakest of hydrogen bonds that occurs between C–H groups and electron pairs in a π system.Various types of supramolecular interactions are shown in the Figure 2.

Chapter 2: Literature Review

2. Literature Review

A short review on "Metal chelating properties of hydroxyquinolines and its derivatives and biological activities"

8-Hydroxyquinoline (8HQ) (Fig. 3), a quinoline derivative originating in plants as well as from synthesis, has been used as a fungicide in agriculture and a preservative in the textile, wood, and paper industries.1(Short,Vargas Thomas 2006) 8HQ possesses potent coordinating ability and good metal recognition properties, which means it is widely used for analytical and separation purposes as well as for metal chelation.2 (Albrecht M, Fiege M 2008),8HQ is the only one, among seven isomeric monohydroxyquinolines, capable of forming complexes with divalent metal ions through chelation.6(Rubbo SD 1950) Most bioactivities of 8HQ and its derivatives originate from their chelating ability.

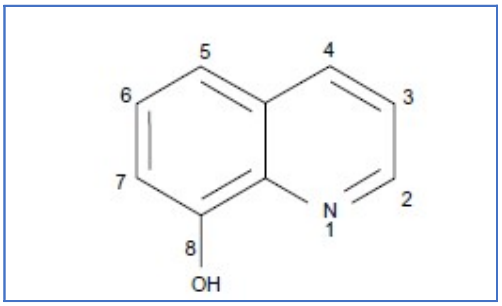


Fig 3.Structure of 8-hydroxyquinoline

A. Antineurodegenerative activity:

A series of 8HQ derivatives, such as 5-chloro-7-iodo-8-hydroxyquinoline, or clioquinol (CQ), 5-((4-(prop-2-ynyl)piperazin-1-yl)methyl)quinolin-8-ol (HLA-20), 5-((methyl(prop-2-ynyl)amino)methyl)quinolin-8-ol (M30), and 5-((4-(2-hydroxyethyl)piperazin-1-yl)methyl)quinolin-8-ol (VK-28) (Fig. 4), have been reported to exert potent antineurodegenerative effects.15(Zheng H, Gal S, Weiner LM2005,) Among these, CQ has reached pilot Phase II of clinical trials in Alzheimer's disease (AD), patients.16–20

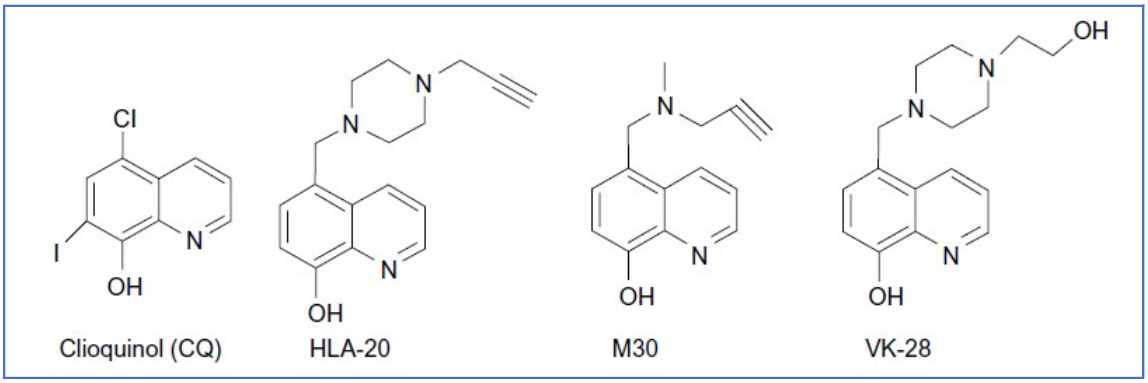


Fig. 4 8-Hydroxyquinoline derivatives with potent antineurodegenerative activity.

The compounds M30 and HLA-20 (Fig. 5) are novel multifunctional 8HQ-based drugs synthesized by combining an Fe chelating compound possessing an antioxidant activity (VK-28) with the Parkinson's drug (Ladostigil) containing the N-propagylamine moiety (Fig. 5), which affords the neuroprotective property.34 (Pollak Y, Mechlovich D, Amit T 2013).

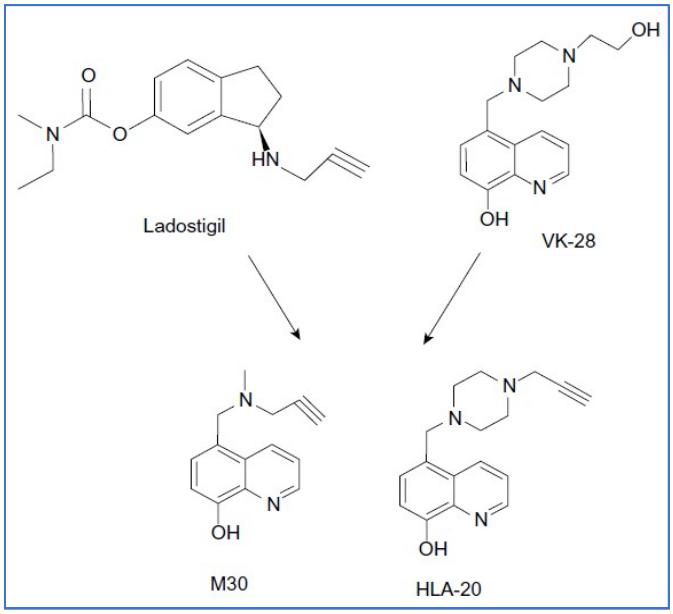


Fig. 5.M30 and HLA-20 are hybrids of Ladostigil and VK-28.

B.Anticancer activity

In addition, metal complexes of mixed ligands of 8HQ-uracils (Fig. 6) have been reported to provide significant cytotoxicity against human cancer cells (ie, HepG2, A549, HuCCA-1, and MOLT-3).63 (Prachayasittikul S, Worachartcheewan A, Pingaew R2012), The anticancer effects of 8HQ derivatives, such as CQ, are related to Cu and Zn ions. As a Cu chelator, CQ

exerts selective antiangiogenesis activity80 toward breast cancer81, prostate cancer,79(Chen D, Cui QC, Yang H2007), leukemia, and myeloma,82(Mao X, Li X, Sprangers R2009), with less effect on normal cells. In addition, the antitumor activity of CQ has been proposed to be tightly associated with proteasome inhibitory ability,79 (Chen D, Cui QC, Yang H2007,) which is elicited through ionophore actions.

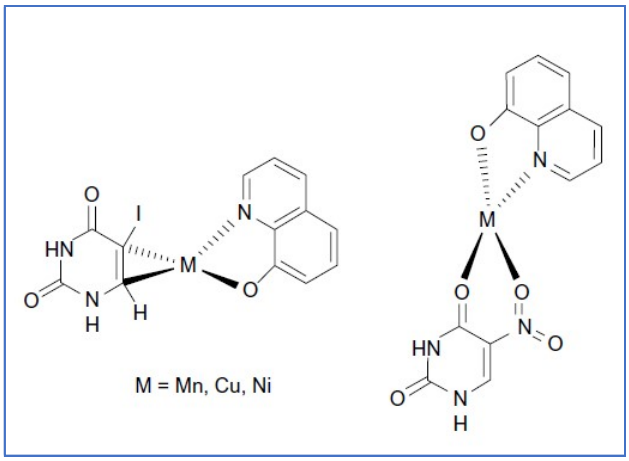


Fig. 6 .Structure of 8-hydroxyquinoline-uracil metal complexes.

It is observed that nitro containing 8HQ derivatives such as nitroxoline (8-hydroxy-5-nitroquinoline; NQ) (Fig. 7) exerted more potent anticancer activity, with a IC50 of 5–10-fold less than that of CQ (halogenated 8HQ derivative), and may be less neurotoxic.96Recently, glucoconjugates of 8HQ derivatives (Fig. 8) were developed as anticancer prodrugs in order to improve the selectivity and to avoid chelation of systemic metal ions.99 (Oliveri V, Giuffrida ML, Vecchio G, Aiello C, Viale M 2012) It was reported that glucose avidity, increased glycolysis rate, and overexpression of glucose transporters were found in cancer cells.100(Kawamura T, Kusakabe T, Sugino T,2001)

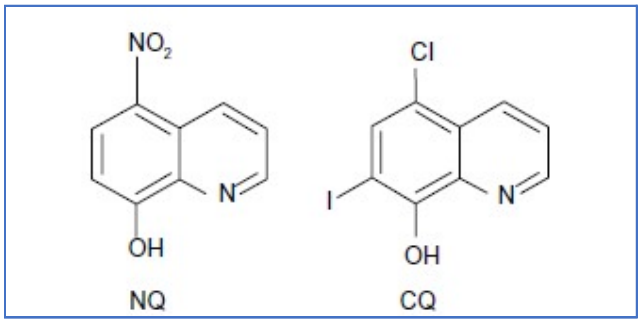


Fig. 7 Chemical structures of nitroxoline (NQ) and clioquinol (CQ).

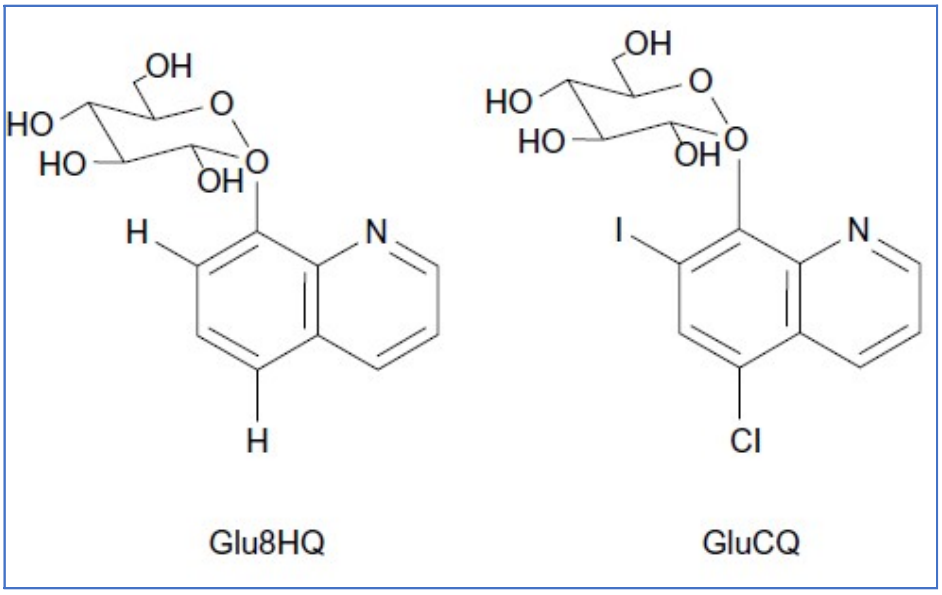


Fig. 8. Glucoconjugates of 8-hydroxyquinoline and clioquinol

Abbreviations: Glu8HQ, glucoconjugate of 8-hydroxyquinoline; GluCQ, glucoconjugate of clioquinol.

C. Antimicrobial activity:-

Antimicrobial effects of 8HQ and its derivatives encompassing antibacterial, 102–104 antimalarial, 105–107 antiviral, 108 antitubercular, 109 and antidental plaque activities110, 111 have been previously reported

4-benzenesulfonamide (HQMABS), shown in (Fig. 9), is a hybrid of 8HQ and sulfanilamide and was reported to be a ligand for metal complexes.5(Vanparia SF, Patel TS, Sojitra NA2001,) This study showed that HQMABS exhibited more potent antimicrobial activity with higher sensitivity against Gram-positive bacteria as compared to their individual parent compounds (ie, 8HQ and sulfanilamide).58HQ-uracil metal complexes bearing antimicrobial activity (Fig.9) have been reported.121 (Srisung S, Suksrichavalit T, Prachayasittikul S, Ruchirawat S, Prachayasittikul V.)

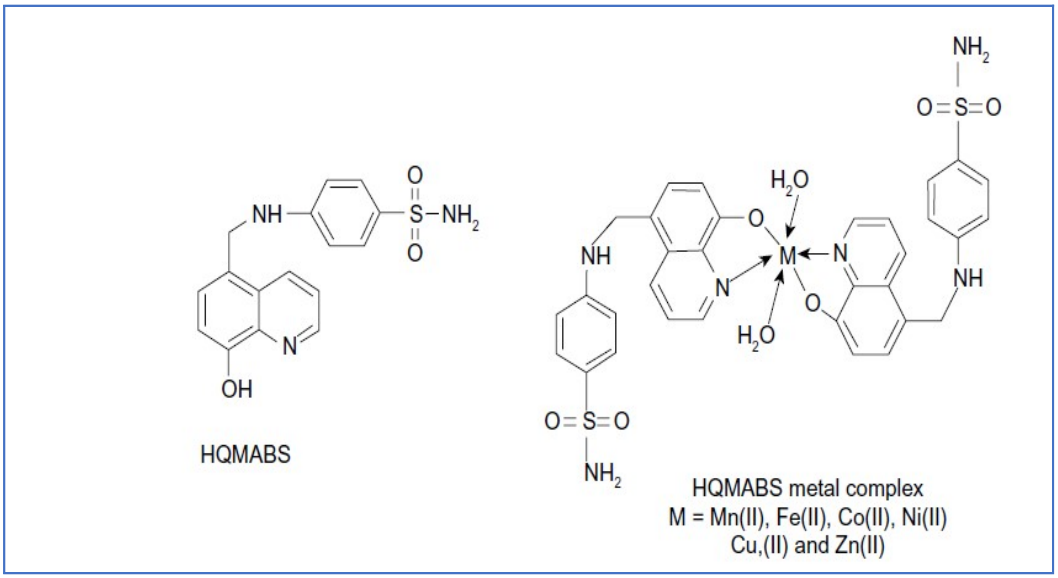


Fig 9. Chemical structures of HQMABS and metal complexes.
(Abbreviation:HQMABS, 4-benzenesulfonamide)

D. **Antiviral activity:**

It is well recognized that nucleic acid binding ability is important for RNA-dependent-DNA polymerase inhibition, which is essential for antiviral activity.124 (Rohde W, Mikelens P, 1976) Among the groups of tested metal-binding compounds, 8HQ exhibited high antiviral activity with approximately 50-fold higher activity.124 (Rohde W, Mikelens P, Jackson J, Blackman J, Whitcher J, Levinson W.) Moreover, the binding activity of the Cu complexes of 8HQ and its derivatives were significantly higher than their respective free ligand forms.124(Rohde W, Mikelens P, Jackson J, Blackman J, Whitcher J, Levinson W.1976)

E. Antioxidant activity

8HQ derivatives have been reported as potent antioxidants,32,37,152,153 which arises from their chelating ability.A series of mixed ligand metal complexes using 8HQ, 5-iodouracil, and 5-nitrouracil as ligands were synthesized and studied for their antioxidant activity using SOD assay.63(Prachayasittikul S, Worachartcheewan A, Pingaew R2012), The results showed that amongst the different tested metal complexes, the 5-iodouracil-Mn-8HQ complex was shown to exert the highest activity, with a IC50 of about 3-fold less than that of the free ligand 8HQ.63

F. Anti-inflammatory activity

8HQ inhibits nitric oxide production at transcriptional level via inhibition of NF-κB and C/EBPβ DNA binding. So, 8HQ possesses anti-inflammatory activity.

Chapter 3: Aims and Objective

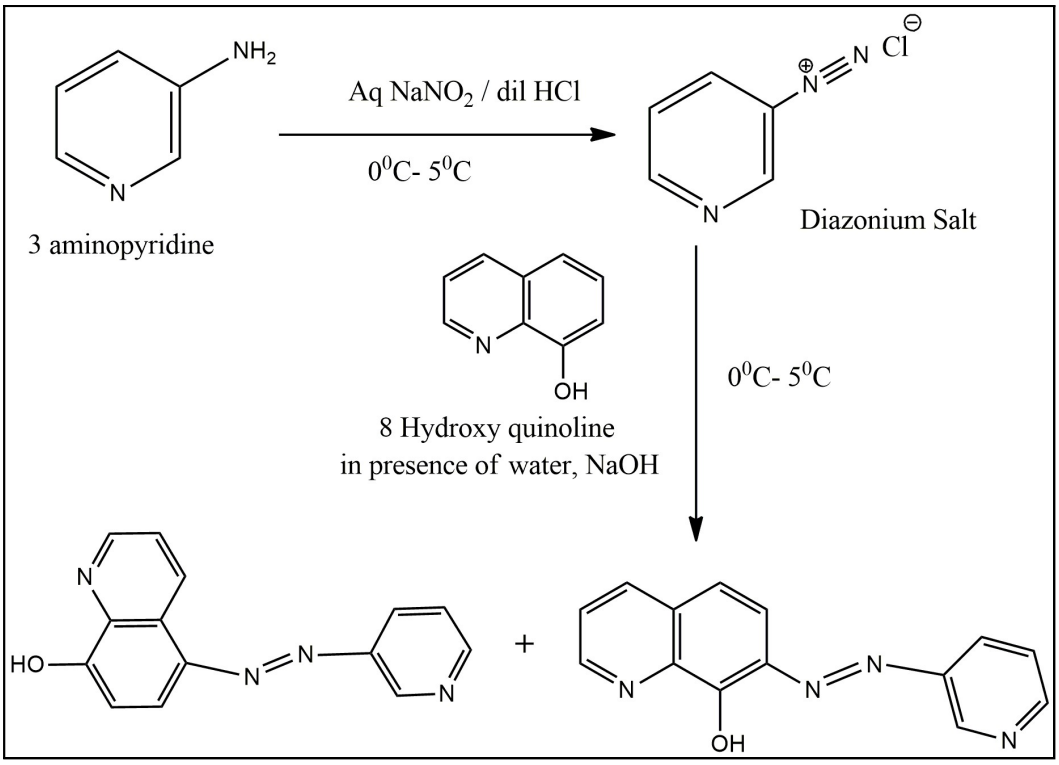
Aims:

The aim of this thesis is to investigate and develop Synthesis of Metal Complexes of Azo Dye Ligands and Characterization of this ligands.

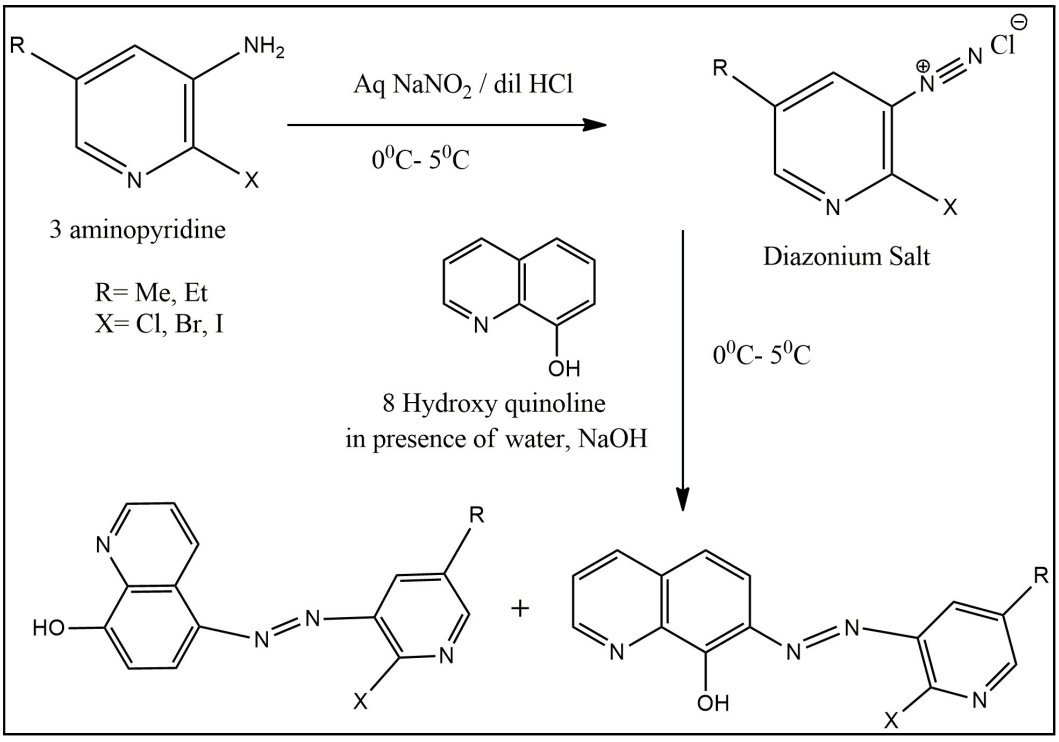
Objectives:

- Synthesis a series of multidentate Azodye ligands of suitably positioned donor sites.
- Following the synthesis of the compounds, they will be thoroughly characterized by standard analytical techniques, viz. elemental analysis, X-ray diffraction analysis (XRD), FTIR study.
- Syntheses of transition metal complexes, spectroscopic and electrochemical characterization of the synthesized metal complexes, preparation of single crystals and single crystal X-ray structure determination of these synthesized complexes.
- The biological activity of synthesized complexes will be examined under various conditions.
- Finally, it will be tried to explore supramolecular features of synthesized metal complexes. The outcome of the proposed project work will be submitted in various journals of repute for publication.

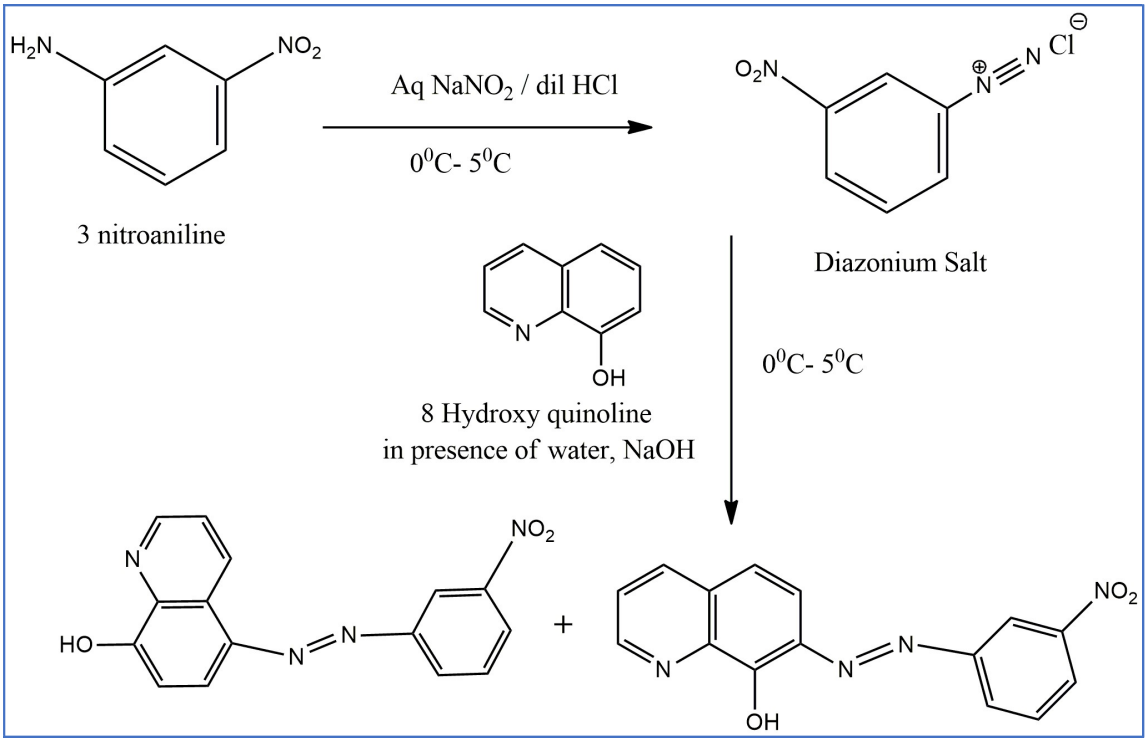
Scheme 1: Synthesis of azo dye ligands of 3-aminopyridine



Scheme 2:Synthesis of azo dye ligand of 3-aminopyridine derivetives



Scheme 3:Synthesis of azo dye ligand of 3-nitroaniline



Chapter 4: Materials and Mehods

4. Materials:

First row transition metal salts of Co, Cu, Ni, Zn, Mn, Fe, (like nitrates, chlorides, carbonates, perchlorates etc.). 2-aminopyridine, 3-aminopyridine, 4-aminopyridine and their derivatives. 8-hydroxyquinoline and its derivatives. 3-nitroaniline, 2-nitroaniline, anilinehydrochloride, 2-amino phenol, 4-nitroaniline etc.

5. Methods:

A. Experimental Procedure:

(a)Purchase of chemicals.

(b)Experimental instrument set up.

(c) Synthesis of compound (chemical reaction).

(d) Purification of compounds.

(e) Preparation of single crystals.

(f) Structure determination.

(g)Characterization of synthesized compound.

B. Instrumentation for experiments and characterization

Characterization techniques

Elemental analysis

- CHNS Analyzer

Structural Analysis

- Fourier Transform Infra-Red Spectrometry (FTIR)
- X-ray Diffraction Spectrometry (XRD)

Thermal Analysis

- Thermo Gravimetric Analyser (TGA)
- Differential Thermal Analyzers (DTA)

Interaction Analysis

- DFT calculation
- NCI analysis
- Hirshfeld surface analysis

C. Project Schedule of project work.

Sl. No.	Activity Description	Project Schedule Number of Weeks 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
1	Project Initiation and Planning	■																							
2	Step I Literature survey or review work		■	■																					
3	Step II Research problem finalized				■	■																			
4	Step III Experimental instrument set up						■	■																	
5	Step IV Synthesis of compound								■	■	■	■													
6	Step V Purification of compounds												■	■											
7	Preparation of single crystals														■	■	■								
8	Final Report																	■	■	■					
9	Implementation																				■	■			
10	Final inspection																						■	■	■

D. Estimation

Item	Expenses
A. Recurring:	
1.Remunerations/salaries	
2.Consumables Chemicals: Metal salts of Co, Cu, Ni, Zn, Mn, Fe, (like nitrates, chlorides, carbonates, perchlorates etc.). 2-aminopyridine, 3-aminopyridine, 4-aminopyridine and their derivatives. 8-hydroxyquinoline and its derivatives. 3-nitroaniline, 2-nitroaniline, anilinehydrochloride, 2-amino phenol, 4-nitroanilineGlassware: 100ml beaker 20pcs., watch glass, Condenser, Distillation set u Chemicals and Glassware	15000.00 3000.00
4. Other costs	2000.00
B. Non-recurring Permanent equipment PH meter, Magnetic stirrer & heater.	 3995.00 4100.00
Grand Total (A+B)	28095.00

Chapter 5: Results

6. Results:

Synthesis of new Azo Dye Ligand.

8- Hydroxy quinolone basaed AzoDye Ligand have been prepared via coupling of the diazoniumsolt of 3-aminopyridine with a basic solution of 8- hydeoxy quinolone . The diazonium salt is prepared by dissolving of the 3-Aminopyridine (0.5g) in dil. acidic mixture (15ml 6M HCL), then cooling at 0^0-5^0C then Sodium nitite solution (1g in mi D.W) was added slowly with stirring and cooling in(0^0-5^0 C) and left for 15 min for diazoniumpreparing.While coupling component was prepared by dissolving eqi-molal quantity(0.5g) 8- hydroxyl quinolone in 10% basic NaOH solution and cooling at same tempareture. When diazoniumsolt prepare, it dropped with stirring and cooling to the coupling component . As a result a red dye was observed .The pH value must be adjusted to complect this reaction. The red Dye was filtered and stored.

7. UV Spectroscopy Data:

We Collected the UV spectra data for this new Azo Dye Ligand by using 60UV- Vis spectrophotometer has a wavelength range of 190–1100 nm.

We took the UV data for 3-aminopyridine , 8-hydroxy quinolineseparetly.

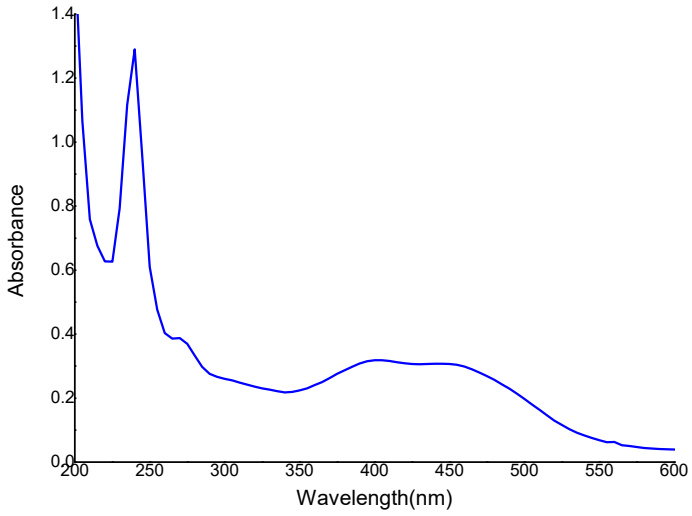


Fig. 10. UV plot of 3 -Aminopyridine

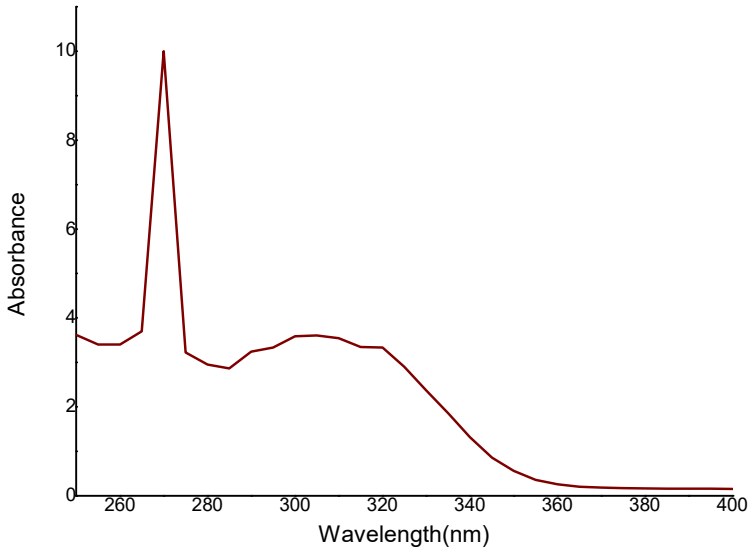


Fig. 11. UV plot of 8 -HydroxyQuinoline

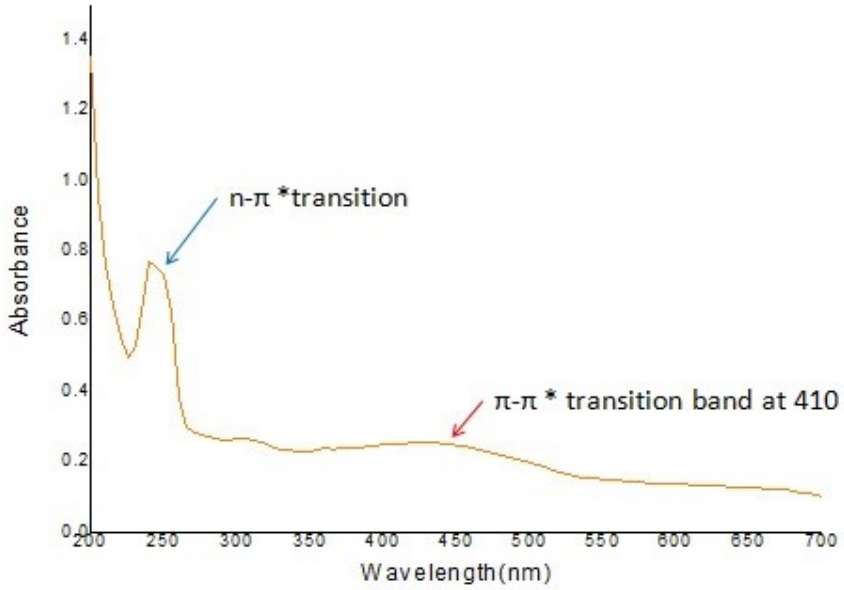


Fig.12. UV plot of synthesized ligand

Chapter 6: Discussion

8. Discussion:

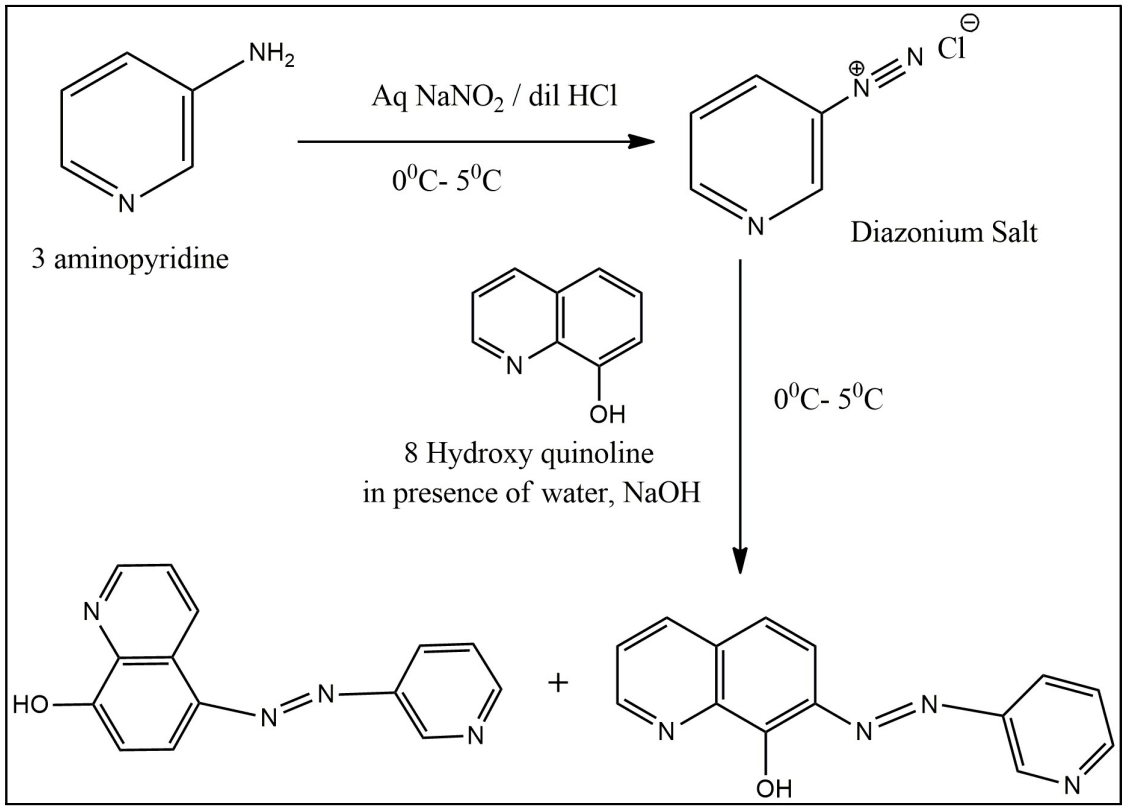


Fig. 13: Structure of the new Synthesized compound characterized by UV study.

Azo dyes contain intermolecular charge-transfer chromophores and therefore, their UV–VIS absorption bands depend on the combination of electron-donating and -withdrawing moieties in the molecules.

Form the **Fig.12.** displays a significant π-π * transition band at 408 nm and a weak sub-band at 461 nm corresponding to the overlap between the n-π * and the vibronic transition bands. So we conclude that depending our results our synthesize product is different as we expected.

Chapter 7: Conclusion

9. Conclusions:

- Supramolecular chemistry is also important to the development of new pharmaceutical therapies by understanding the interactions at a drug binding site.
- From our project work we understand about the different types of non-covalent interaction which is responsible for crystals packing by DFT calculation.
- We can explore supramolecular chemistry include molecular folding, molecular recognition, host- guest chemistry.

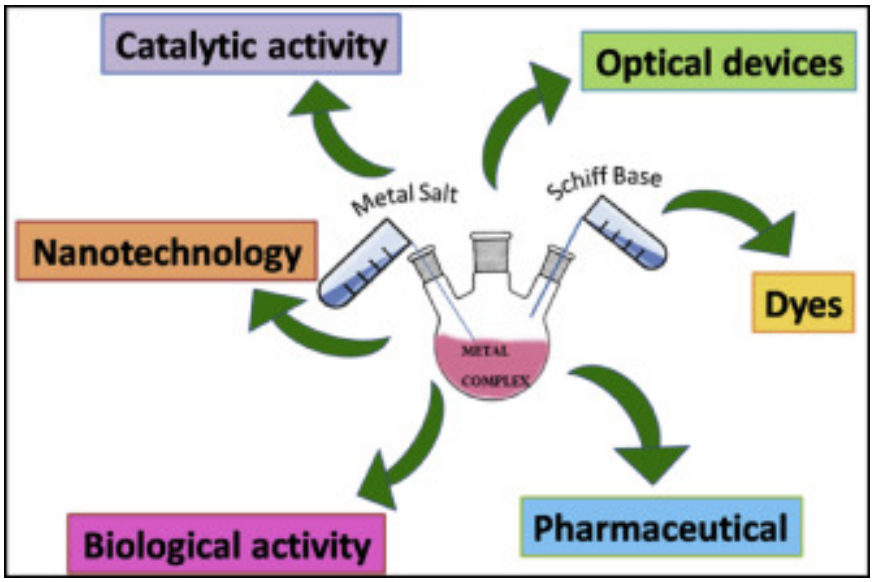
Also, some Schiff base complexes have been used as promising catalysts which could be applied as green chemistry reagents. Furthermore, successful development of such low cost catalytic agents should have tremendous economic values as it relates to trade and industrial production. So our conclusion is that

- Review work has been done.
- Finalization of project work is done.
- Planning of project work has been decided.
- Purchase of chemical and instruments set up is made.
- Some chemical reactions have been performed.
- Chemical reaction is under observations.
- We have synthesized some azo dye ligends.

Chapter 8: Future Scope

10. Future Scope:

Azo dye have been investigated in relation to a wide range of contexts, including antimicrobial, antiviral and anticancer activity**.** Azo dye are common ligands in coordination chemistry



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