Annexure – VIII

UNIVERSITY GRANTS COMMISSION
WESTERN REGIONAL OFFICE
GANESHKHIND, PUNE – 411 007.

PROFORMA FOR SUBMISSION OF INFORMATION AT THE TIME OF SENDING THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

1	Name and Address of the Principal Investigator	**Dr. Khursheed Ahmed** 26/03, Kauser Bagh Society, Knodhwa Khurd, Pune – 411048
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3	UGC Approval No. and Date	F. 47-1135/14 (General/90/WRO) dated 24/03/2017
4	Date of Implementation	24-03-2017
5	Tenure of the Project	2 Years
6	Total Grant Allocated	Rs. 2,40,000/-
7	Total Grant Received	Rs. **1,75,000/-**
8	Final Expenditure	Rs. **1,68,785/-**
9	Title of the Project	Structural Investigations and DNA Nuclease Activities of Schiff Base Copper and Iron Complexes: A Biomimetic Approach
10	Objectives of the Project	1. To synthesize new iron and copper complexes using Schiff's bases L1-L5 of Lawsone. Three Schiff's bases were obtained from Lawsone (2-hydroxy-1, 4-naphthoquinone), three different isomeric methyl pyridine amines and two Schiff's bases were synthesized using different benzohydrazide. 2. To study the *in silico* molecular docking of synthesized Schiff Bases (L1-L5). 3. To elucidate the electronic structures of M1-M5 by using C, H, N analysis, TGA, Cyclic Voltammetry (CV) and IR, UV, EPR spectroscopic characterization. 4. To study the bio-functionalities of synthesized complexes in terms of antioxidant and quantitative DNA cleavage studies.

		6. To propose a suitable and proper mechanism for the DNA nuclease activities of metal complexes.
11	Whether Objectives Were Achieved (Give Details)	Yes, The grant was received only for one year. Five ligands and iron complexes from these ligands were synthesized. The chemical structures of ligands and iron complexes were determined. Two types of functional studies were carried out, one anti-oxidant and the other DNA nuclease activities of iron metal complexes. Please refer the attached report.
12	Achievements From the Project	1. Successfully, five new iron (II) complexes using were synthesized using Schiff's bases **L1-L5** obtained from Lawsone. Three Schiff's bases were obtained from Lawsone (2-hydroxy-1, 4-naphthoquinone), three different isomeric methyl pyridine amines and two Schiff's bases were synthesized using different benzohydrazide. 2. *In silico* molecular docking of synthesized Schiff Bases (**L1-L5**) were carried out. 3. Structural characterization of ligands and complexes were carried out by using various techniques such as C, H, N analysis, TGA, Cyclic Voltammetry (CV) and IR, UV, EPR spectroscopy. 4. The bio-functionalities of synthesized iron complexes were determined in terms of antioxidant properties and quantitative DNA cleavage studies. Please refer the attached report.
13	Summary of the Findings (In 500 Words)	Under specific chemical conditions, five new iron (II) complexes M1-M5 are synthesized using Schiff's bases L1-L5 obtained lawsone. Three Schiff's bases L1-L3 were obtained from Lawsone (2-hydroxy-1, 4-naphthoquinone) and three different isomeric methyl pyridine amines.

		Two Schiff's bases were synthesized using lawsone and two different benzohydrazide. In order to explore the possible target of synthesized derivatives, in silico molecular docking studies were carried out on the crystal structure of Topoisomerase 2 (3Qx3). The important binding interactions of the actively docked conformations of ligands with the target proteins are identified. The results have shown strong hydrogen bonding and hydrophobic interactions with the target protein. Theoretical studies showed that the binding energy of L-3 is the lowest which means among the five ligands, L-3 could be the most potent anticancer drug. The electronic structures of iron complexes M1-M5 were determined by using C, H, N analysis, TGA, Cyclic Voltammetry (CV) techniques and IR, UV, EPR spectroscopic characterization. Two different types of bio-functionalities of synthesized complexes were studies, one in terms of antioxidant properties and the second the quantitative DNA cleavage studies. In UV visible spectroscopy, the observed absorption peaks in the electronic spectra between 400-590 nm suggest distorted octahedral geometries of compounds. M-1 showed two peaks at 458 nm and 590 nm. The absorption peak at 458 nm corresponds to t2g → a1g* transition while the second peaks at 590 nm is due to t2g→ eg* transitions. In IR free quinone νs C=O appears in the range of 1660-1700 cm−1. A downward shift of ~ 10 cm−1 occurs if the quinone is coordinated as ortho-quinone (o-quinone) tautomer in its fully oxidized form. The observed IR frequencies near 1580 cm−1 in all complexes again confirm the mixed valence forms of naphthoquinone (quinone and semiquinone forms) and counter

		balance the metallic positive charges to produce neutral compounds. From the kinetic data of thermal analyses of iron complexes, the activation energies in M1- M5 obtained for various decomposition steps are close to 25 kJ/mol and 60 kJ/mol. Hence, we concluded that all synthesized compounds possess mixed valent tautomeric ligation. Similarly, observed values of activation energies of ligands obtained from TGA data indicate presence of Schiff's bases containing quinone and naphthosemiquinone forms of Lawsone. Ain CV a redox couple is observed in all metal complexes at E1/2 values between 0.250 V to 0.45 V that may be assigned for Fe II/III with ΔE = 0.12 V to 0.16 V for two electron transfer processes. These results confirm that all synthesized metal complexes contain Schiff's bases ligands containing at least one Lawsone into its NSQ state which is its radical form. The antioxidant studies were carried out in terms of DPPH (1, 1-dipheny-2-picryl hydrazyl) radical scavenging activities using the reported procedure. All the compounds ligands and complexes showed better antioxidant activities than standard ascorbic acid. The ligand L1 in the present study shows remarkable reduction of DPPH with IC50 value 10 μM while M3 with lowest IC50 value 8 μM is the most active compound of the series. The physiological activities of M1-M5 were studied in terms of their DNA cleavage activities using pUC-19 DNA. The quantitation of DNA nuclease activities showed that M1 and M2 are better nuclease than other complexes which is ~ 32 %. Enhancement in cleavage activity by M1 and M2 may be related to oxidative mechanism producing less stable non-covalent intermediate

		to initiate the reaction hence role of nitrogen and oxygen containing ligands is thus signified. Finally, we conclude that M1 and M2 acts as better exonucleases performing through hydrolytic mechanism.
14	Contribution to the Society (Give Details)	The synthesized compounds (ligands and iron metal complexes) were in vitro tested for their anti-oxidant and anticancer activities in terms of quantitative DNA cleavage activities. Some of the compounds of this series showed remarkable activities and those could be potential drugs in future.
15	Whether Any Ph.D. Enrolled/Produced out of the Project	NO
16	No. of Publications out of the Project (Please Attach Re-Prints)	NO

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