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Synthesis, Spectral Characterization, Molecular Docking, Antimicrobial And Antioxidant Evaluation Of Pharmacophores 1, 3-Diones with Their Transition Metal Complexes

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ABSTRACT

Three series of 1, 3-diones 4(LA- LC) and their transition metal (II) complexes 5LA (a-e), 5LB (a-e) and 5LC (a-e) have been synthesized, spectroscopically characterized and their in vitro efficacies were evaluated. Bidentate ligands were derived from substituted aromatic acids and substituted ortho hydroxy acetophenone under ultrasound irradiation methods at low temperature. The simple substitution reactions between the metal nitrate and ligands yielded the titled complexes. However, in situ procedure gives high yield with formation of single products as evident by TLC. Elemental analysis, IR, 1H and 13C-NMR , Masss pectra, UV-Vis., magnetic susceptibility and conductance measurements were done to characterize the ligands and their metal complexes [where, M= Mn (II), Fe (III), Co (II), Ni (II) and Cu (II)]. All the evidences suggested that the complexes have octahedral geometry. The stoichiometry of the complexes was found to be 1:2 (metal: ligand). The conductivity data show that the complexes are non-electrolyte in nature. The antioxidants activity of the ligands and their metal (II) complexes have been carried out using DPPH free radical scavenging activity and found to be most effective. The antibacterial and antifungal activity of the ligands and their complexes have been carried out and on the basis the molecular docking studyagainst the peptide deformylase of the most effective complexes has been reported.

Keywords: 1, 3-diones, Metal complexes, Antimicrobial, Antioxidants and Molecular docking.

I. INTRODUCTION

The coordination chemistry of transition metal (II) complexes with 1, 3-diones as ligands is of current interest because they can provide new materials with useful properties such as antifungal, antibacterial, anticancer [1,2], antisecticidal [3], antioxidant [4], potential prophylactic antitumor activity [5,6], magnetic exchange [7,8], electrical conductivity [9]. The biological importance of metal (II) complexes is that they are sometimes highly effective than the free ligands [10]. Metal complexes containing pyridine and derivatives have aroused considerable interest in view of their industrial and biological importance [11, 12]. They have also been found to be active against influenza and have been suggested as possible pesticides and fungicides. Their activity has been thought to be ability to chelate trade metals [13, 15].

Recently, applications of these transition metal complexes in the design and development of synthetic restriction enzymes, new drugs and stereo selective probes of nucleic acids structure have been explored extensively [16]. Transition metal complexes offer two peculiar advantages as DNA-binding agents [17] and functionality of the binding agent [18] these characteristics have promoted metal complexes used in a wide range of applications [19].

In continuation of our interest in the functionalized 1, 3-diones and their metal (II) complexes, we, herein report the synthesis, spectral characterization, antimicrobial, antioxidants studies of a bidentate ligands containing O, O pharmacophores. The molecular docking study of ligands and their metal complexes has been reported [20-21]. The antibacterial and antifungal activities of ligands and their metal (II) complexes observed that, metal complexes showed highest activity than the free ligands.

II. Experimental

2.1 Materials and Methods

All chemicals used were of the analytical grade. *Ortho* hydroxyacetophenone and 4-nitrobenzoic acid were SD fine products and used as supplied. The UV-Vis spectra of the ligands and their complexes were recorded on Shimadzu UV-1800 Spectrophotometer. IR spectra were recorded on Shimadzu FT-IR-4100 spectrometer using KBr pallets. ^{1}H-NMR spectra of the ligand was recorded using a Bruker DRX-500 MHz NMR spectrometer. Mass spectra were taken on a Macro Mass spectrometer.

2.2 Synthesis of 2-acetylphenyl benzoate3(a-c):

To the reaction mixture of substituted *ortho* hydroxy acetophenone (1.70 g, 0.01 mol) and substituted benzoic acid (1.66 g, 0.01 mol), a dry pyridine (5mL) and $POCl_3$ (1mL) were added drop wise maintaining temperature 0 ^{0}C.Then the reaction mixture was irradiated for about 2-3h under ultrasound. After completion of the reaction (monitored by TLC), the mixture was poured into 100ml 1M HCl containing 50 gm crushed ice with vigorous stirring. The crimson colored solid (ester) was obtained which was filtered and washed several times with ice-cold methanol. It was crystallized with distilled ethanol.

2.3 Synthesis of Ligands 4(L_A-L_C)

2.3.1 Synthesis of 1-(2-hydroxyphenyl)-3-(4-nitrophenyl) propane-1, 3-dione 4(L_A):

A Compound (**3a)** was dissolved in 15 ml dry pyridine. To this mixture, powdered KOH was irradiated for about 1-2 h. Then it was poured over crushed ice and acidified with conc. HCl. The resulting solid **4(L_A)**was recrystallized from ethanol (Yield: 82%); m.p.132 ^{0}C.)^{1}H-NMR, 14.80δ (s, 1H, enolic -OH), 11.87δ (s, 1H, Phenolic –OH) 7.49δ (s, 1H, =C-H ethylene), 6.54-7.98δ (m, 8H, Ar-H); IR (KBr) ν_{max}/cm^{-1}; 1735 (ν (C=O) ketonic), 1199 (ν (C-O) enolic), 3099 (ν (-OH) intramolecular H-bonding in Phenolic). UV/Vis. (DMSO) nm: 399, 340. MS *m/e*: 285.06

2.3.2 Synthesisof1-(5-bromo-2-hydroxyphenyl)-3-(4-fluorophenyl) propane-1, 3-dione 4(L_B):

A Compound containing (**3b)** 3.18 g, 0.01 mol) was dissolved in 15 mL dry pyridine. To this mixture, powdered KOH (1.12 g, 0.02 mol) was irradiated for about 1-2 hrs. Then it was poured over crushed ice and acidified with concentrated hydrochloric acid. The resulting solid **4(L_B)**was recrystallized from ethanol (Yield: 80%);m.p.:172^{0}C. ^{1}H-NMR (500 MHz, $CDCl_3$-d_6); δ /ppm = 15.56 (s, 1H, enolic -OH), 12.02 (s, 1H, Phenolic –OH), 7.55 (s, 1H, =C-H ethylene), 6.72-8.02 (m, 7H, Ar-H). ^{13}C-NMR (500 MHz, $CDCl_3$) δ/ppm = 194.17 (C=O), 177.35 (C-O enolic), 91.85 (=C-H ethylene).IR (KBr) ν_{max}/cm^{-1}; 1744 (ν(C=O) ketonic), 1178 (ν (C-O) enolic), 3109 (ν (-OH) intramolecular H-bonding in Phenolic). UV/Vis. (DMSO) nm: 371, 256. MS *m/z*: 337.98.

2.3.3 Synthesis of 1-(2-hydroxyphenyl)-3-(4-t-butylphenyl) propane-1, 3-dione4(L_C):

A Compound(**3c)**was dissolved in 15 ml dry pyridine. To this mixture, powdered KOH was irradiated for about 1-2 h. Then it was poured over crushed ice and acidified with conc. HCl. The resulting solid **4(L_C)** was recrystallized from ethanol (Yield: 82%); m.p.122 ^{0}C.)^{1}H-NMR, 11.35δ (s, 1H, Phenolic –OH) 7.99δ (s, 1H, =C-H ethylene), 6.98-8.09δ (m, 8H, Ar-H), 1.31δ (s, 9H, t-butyl group);IR (KBr) ν_{max}/cm^{-1}; 1688 (ν (C=O) ketonic), 1235 (ν (C-O) enolic), 3025 (ν (-OH) intramolecular H-bonding in Phenolic). UV/Vis. (DMSO) nm: 369, 256.

2.4 Synthesis of metal complexes

The metal complexes were prepared by the hot solution of the appropriate metal nitrate (10 mmol) in ethanol (25ml) to the hot solution of the ligands **4(L_A-L_C)** (10 mmol) in the same solvent. The resulting mixture was irradiated for about 1h under ultrasound whereupon the complex precipitated. They were collected by filtration, washed thoroughly with ethanol and dried in vacuum.

2.4.1Ana. Calcd. for5L_A (a-e):

(Yield: 80-85%) IR (KBr) ν_{max}/cm^{-1}; 1680-1665 (ν(C=O) ketonic), 1203-1209 (ν(C-O) enolic), 3072 (ν (-OH) intramolecular H-bonding in Phenolic), 3435-3462 (ν (-OH) in H_2O molecules) 450-465 (ν (M-O bond in complex);UV/Vis. (DMSO) nm: 271 ($\pi \rightarrow \pi^*$),398 (LMCT) , 672-674 (d-d transition).

2.4.2 Ana. Calcd. for5L_B (a-e):

(Yield: 80-82%) IR (KBr) ν_{max}/cm^{-1}; 1649-1645 (ν (C=O) ketonic), 1143-1149 (ν (C-O) enolic), 3072-3030 (ν (-OH) intramolecular H-bonding in Phenolic), 3464-

3367 (ν (-OH) in H_2O molecules) 526-513(ν(M-O bond in complex); UV/Vis. (DMSO) nm: 271(π→ π*),398(LMCT) , 670-674 (d-d transition)

2.4.3 Ana. Calcd. for$5L_C$ (a-e) :

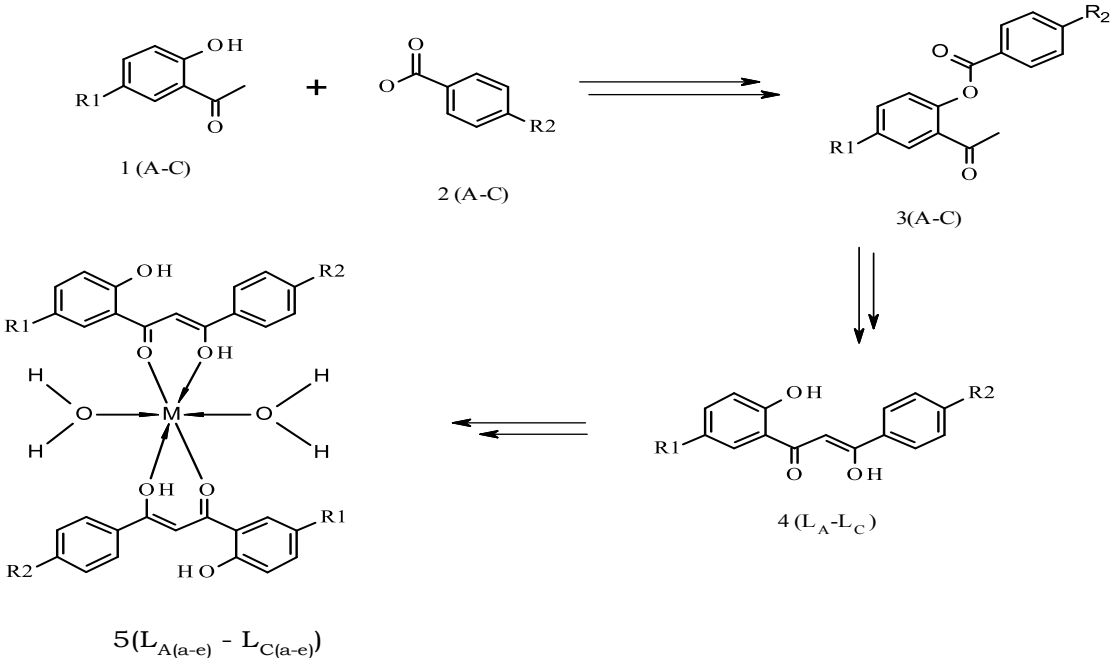
(Yield: 82-87%) IR (KBr) ν_{max}/cm^{-1}; 1590-1631 (ν(C=O) ketonic), 1126-1198 (ν(C-O) enolic), 2957-3009 (ν (-OH) intramolecular H-bonding in Phenolic), 550-565 (ν (M-O bond in complex); UV/Vis. (DMSO) nm: 256-267 (π→ π*),369-376

III. Results and discussion

1, 3-diones was prepared by the esterification of substituted 2-hydroxy acetophenones **1(A-C)** with substituted aromatic acid **2(A-C)** in presence of $POCl_3$ (Scheme 1) to afford **3(A-C**) which upon subsequent treatment with KOH afforded yellow solid **4(L_A-L_C).** All the complexes **5L_A (a-e), 5L_B (a-e)** and **5L_C (a-e)**were colored solids, air stable and soluble in polar solvents like DMF and DMSO. The elemental analysis show 1:2 (metal: ligand) stoichiometry for all the complexes. The structures of the compounds were characterized by spectral analysis. The magnetic measurement studies showed that the complexes **5(a-e)** have octahedral geometry.[22] All complexes showed higher antibacterial activity than the free ligands. Antioxidants results were more effective.

3.1 Synthesis of 1, 3-diones

Scheme: I



Reaction Conditions: i) $POCl_3$ / Py / Ultrasound irradiations

ii) KOH / Py / Ultrasound irradiations

Compounds	R_1	R_2
4 (L_A)	-H	$-NO_2$
4 (L_B)	-Br	-F
4 (L_C)	-H	-t butyl

M:

a Mn (II)
b Fe (II)
c Co (II)
d Ni (II)
e Cu (II)

3.2 Conventional and ultrasound irradiation techniques

Table 1. Physical Characterization and ultrasonic study of ligands and their metal complexes.

Ligands/Complexes	Mol.Wt.	M.P./decomp. Temp (^{0}C)	Conventional		Ultrasound Irradiation [a]	
			Time (min)	Yield (%)	Time (min)	Yield (%)
$4L_A$	285.25	132	370	70	120	82
$5L_A$(a)	659.46	272	280	72	90	80
$5L_A$(b)	660.36	324	280	68	90	84
$5L_A$(c)	663.45	268	280	70	90	85
$5L_A$(d)	663.21	213	280	**73**	90	**83**
$5L_A$(e)	668.06	239	280	**74**	90	**85**
$4L_B$	337.14	172	370	68	120	80
$5L_B$(a)	763.23	≥300	280	72	90	82
$5L_B$(b)	764.14	≥300	280	68	90	80
$5L_B$(c)	767.23	≥300	280	70	90	85
$5L_B$(d)	766.99	≥300	280	**71**	90	**84**
$5L_B$(e)	771.84	≥300	280	**74**	90	**86**
$4L_C$	296.36	122	370	70	120	82
$5L_C$(a)	681.67	267	280	67	90	80
$5L_C$(b)	682.58	291	280	65	90	84
$5L_C$(c)	685.22	287	280	69	90	79
$5L_C$(d)	685.43	292	280	**70**	90	**85**
$5L_C$(e)	690.28	266	280	**72**	90	**87**

[a] Ultrasound irradiation method has improved yields than the conventional method

The reactions under ultrasound irradiation assisted organic synthesis is an efficient and eco-friendly synthetic strategy for improve yields and increases selectivity. The result shows that the metal complexes of Ni (II) and Cu (II) have highest yields than the others metal (II) complexes.

3.3Magnetic measurements

The magnetic measurements of complexes were measured at room temperature. The observed magnetic moment value of **(5a)** complex is 5.86 BM, **(5b)** complex is 6.33 BM, **(5c)** complex is 4.26 BM, **(5d)** complex is 2.50 BM, and **(5e)** complex is 2.12 BM. The magnetic measurement studies showed that the all complexes have octahedral geometry.[23-26]

3.4 Spectroscopic analysis

The ^{1}H-NMR spectrum of the compound **4(L_A-L_C)** exhibited a singlet at δ 15.56 and 14.80 ppm due to enolic proton a singlet at δ 12.02, 11.87 and 11.87 ppm due to phenolic proton adjacent to the carbonyl group and a singlet at δ 7.55, 7.49 and 7.99ppm respectively showed ethylene proton indicate that keto- enol form in 1,3-diketone is more stable. The characteristics infrared spectral assignment of ligand **4(L_A-L_C)** and their metal complexes **5(a-e)** the presence of broad band at 3030-3072cm^{-1} exhibited intramolecular hydrogen bonding due to –OH group. All the above evidences were further supported by the emergence of new bands at 513-526 cm^{-1} due to metal-oxygen vibrations. These new bands observed in the spectra of the transition metal complexes and not in ligands.

3.5 Antioxidants Activities

An aliquot of 0.5 ml of sample solution (0.2, 0.4, 0.6, 0.8, 1 mg/ml) was combined with 5 ml reagent solution (0.6 M sulfuric acid, 28 mM sodium phosphate and 4 mM ammonium molybdate). The tubes were capped and incubated in a boiling water bath at 95^{0}C for 90 min. After the samples had cooled to room temperature, the absorbance of the aqueous solution of each was measured at 695 nm against blank in Spectronic 20 visible spectrophotometer. A typical blank solution contained 5 ml of reagent solution and the appropriate volume of the same solvent (methanol) used for the sample and it was incubated under same conditions. For samples antioxidant capacity is expressed as equivalents

of ascorbic acid and butyrate hydroxy toluene (BHT) as a reference standard. The ligands **4(L_A), 4(L_B) and 4(L_C)** shows that higher antioxidants capacity than the corresponding metal (II) complexes in terms of IC50.

3.6 Antibacterial and antifungal activities

The present paper is focused on the newly synthesized ligands **4(L_A), 4(L_B)** and **4(L_C)** and their metal (II) complexes **5L_A (a-e), 5L_B (a-e)** and **5L_C (a-e)** as possible antibacterial and antifungal agents. The minimum inhibitory concentrations (MICs, mg/mL^{-1}) of tested compounds against certain bacteria and fungi are shown in table 2. A series of synthesized compounds were prepared and tested for their in vitro antimicrobial activity against the four strains of bacteria (gram +ve, gram –ve), and one strain of fungi (*Candida Albicans*). Four compounds of the obtained series **5L_A (b), 5L_A (d), 5L_B (b)** and **5L_C (e)** showed excellent antibacterial activity against *Escherichia coli* and *Pseudomonas aeruginosa.* The compounds **5L_A (c), 5L_A (d), 5L_B (a), 5L_B (b), 5L_C (a)**and**5L_C (c)**showed that high activity against *Staphylococcus aureus* and *Bacillus Subtilis* as compared to the standard drug *Ciprofloxacin.* The compounds **5L_A (b), 5L_B (b), 5L_B (e),** and**5L_C (a)** showed excellent antifungal activity against *C. Albicans*as compared to the standard drug *Fluconazole*. The compounds were added in nutrient broth medium with bacterium and incubated on a rotary shaker at 37 °C for 24 h at 150 rpm. The percentage growth was calculated by the following equation.[27]

$$\% \text{ Growth} = (\text{OD at 600nm sample} / \text{OD at 600 nm control}) \times 100$$

Table 2. Antimicrobial and Antioxidants activity of compounds. Minimum inhibitory concentrations (mcg/mL^{-1})

Ligands/ Complexes	Antibacterial Activity				Antifungal Activity	Antioxidant Activity
	B. Subtilis **(NICM 2063)**	***S.Aureus*** **(NICM 2079)**	***P.Aeruginosa*** **(NICM 2200)**	***E.Coli*** **(NICM 2065)**	***C. Albicans***	**IC 50**
$4L_A$	197.2	124.4	163.6	156.2	184.2	95.2
$5L_A$(a)	79.6	128.0	99.0	45.4	162.2	40.11
$5L_A$(b)	74.8	135.5	101.0	62.3	162.2	46.35
$5L_A$(c)	57.2	151.0	65.0	89.5	148.0	79.47
$5L_A$(d)	106.4	97.7	110.0	77.4	55.0	21.25
$5L_A$(e)	123.3	79.6	76.0	102.4	104.2	78.49
$4L_B$	143.1	178.1	191.3	187.5	164.9	108.3
$5L_B$(a)	181.4	85.4	69.6	56.1	42.8	10.76
$5L_B$(b)	188.7	82.7	120.4	41.1	164.3	19.47
$5L_B$(c)	135.3	74.1	93.9	105.8	*	28.45
$5L_B$(d)	49.4	108.7	72.6	*	158.4	93.47
$5L_B$(e)	44.8	119.1	59.8	*	179.6	88.91
$4L_C$	166.1	147.9	109.1	102.5	174.2	129.2
$5L_C$(a)	120.4	61.3	43.5	65.1	187.2	*
$5L_C$(b)	105.9	90.6	45.4	84.4	146.6	17.74
$5L_C$(c)	92.9	158.6	89.3	56.8	*	92.54
$5L_C$(d)	76.5	109.3	*	168.2	141.3	*
$5L_C$(e)	94.1	117.2	175.3	39.4	94.2	74.64
Ciprofloxacin	50.0	25.0	50.0	25.0		
Fluconazole					50.0	
BHT						16.50
Ascorbic acid						12.80

*No activity reported up to 200 mcg /mL

IV. Conclusion

The functionalized 1, 3-diones **4(L_A), 4(L_B)** and **4(L_C)** and their metal (II) complexes **5L_A (a-e), 5L_B (a-e)** and **5L_C (a-e)** were characterized by spectral and elemental analysis. All the evidences suggested that the complexes have octahedral geometry. The stoichiometry of the complexes was found to be 1:2 (metal: ligand). The conductivity data show that the complexes are non-electrolyte in nature. The synthesized compounds were studied theoretically for prediction of bioactivity and verified experimentally. All the compounds were screened for antimicrobial and antioxidant activity. The compounds **5L_A (b), 5L_A (c), 5L_A (d), 5L_B (a), 5L_B (b), 5L_C (a)** and **5L_C (e)** were found to be potent antibacterial and antifungal agents comparable with *ciprofloxacin*. The newly synthesized compounds **4(L_A), 4(L_B) and 4(L_C)** were also shown to have the promising antioxidant activity. Molecular docking study corroborates the experimental antimicrobial activity specifically against E. coli. In the docking studies against E. coli peptide deformylase enzyme, the importance of ligand complex's access to deeper binding pocket is revealed. It can be also concluded from docking studies that the presence of electronegative substituent's like bromo, fluoro enhances the antimicrobial activity. On the basis of hypothesis based on Petra, it is found that, these compounds could form the highly interesting combined two or more pharmacophores sites in one molecule. Thus, it is concluded that the compounds were found to possess a broad range of hydrophilic and lipophilic characters; hence indication of favorable bioavailability based on drug likeness [29, 30].It is predicted that most of these compounds could be used without risk of toxicity as diverse antibacterial and antioxidant agents.

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VI. REFERENCES

[1]. X. Xu, T. Xu, J. Gao, M. Wang, S. Niu, S. Ni, G. Xu, Inorg. Met.Org. Nano-Met. Chem. 36 (2006) 681–686.

[2]. C.R. Bhattacharjee, P. Goswami, P. Mondal, J. Coord. Chem. 63 (2010) 2002–2011.

[3]. G.D. Crouse, M.J. McGowan, R.J. Boisvenue, J. Med. Chem. 32 (1989) 2148e2151.

[4]. T. Nishiyama, S. Shiotsu, H. Tsujita, Polym. Degrad. Stab. 76 (2002)435e439.

[5]. N. Acton, A. Brossi, D.L. Newton, M.B. Sporn, J. Med. Chem. 23 (1980) 805e809.

[6]. J. Sheikh, V. Ingle, H. Juneja, E-J. Chem. 6 (2009)705e712.

[7]. R.C. Maurya, P. Sharma, D. Sutradhar, Inorg. Met.Org. Nano-Met. Chem. 33 (2003)669–682.

[8]. Y.T. Li, C.W. Yan, C.Y. Zhu, H.S. Guan, Inorg. Met-Org. Nano-Met. Chem. 34 (2005) 1165–1179.

[9]. Y. Aydogdu, F. Yakuphanoglu, A. Aydogdu, E. Tas, A. Cukurovali, Mater. Lett. 4 (2002)879–883.

[10]. N.S. Youssef, E.A. El Zahany, M.M. Ali, 185 (2010) 2171–2181.

[11]. A. Baxter, C. Bennion, J. Bent, K. Boden, S. Brough, A. Cooper, E. Kinchin, N. Kindon, T. Mcinally, M. Mortimore, B. Roberts, J. Biol. Med.Chem. Lett. 13 (2003) 2625–2628.

[12]. D. Farhanullah, B.K. Tripathi, A.K. Shrivastava, V.J. Ram, Bioorg. Med. Chem. Lett. 14 (2004) 2571–2574.

[13]. B.T. Khan, K. Najmuddin, S. Shamsuddin, S.M. Zakeeruddin, Inorg. Chim. Acta 709 (1990) 129–133.

[14]. B.T. Khan, K. Venkatasubramanian, K. Najmuddin, S. Shamsuddin, S.M. Zakeeruddin, Inorg. Chim. Acta179 (1991) 117–123.

[15]. M.S. Refat, I.M. El-Deen, M.A. Zein, A.M.A. Adam, M.I. Kobeasy, Int. J. Electrochem. Sci. 8(2)

[16]. Y. Tor, Targeting RNA with small molecules, Chembiochem 4 (2003) 998–1007.0139894–9917.

[17]. N. Farrell, in: J.A.McCleverty, T.J. Meyer (Eds.), Comprehensive Coordination Chemistry II, Pergamum, Oxford 2003, p. 809.

[18]. B.M. Zeglis, V.C. Pierre, J.K. Barton, Chem. Commun. 44 (2007) 4565–4579.
[19]. J. Sheikh et al. / European Journal of Medicinal Chemistry 46 (2011) 1390e1399
[20]. V. Thamilarasan et al. / Journal of Photochemistry & Photobiology, B: Biology 160 (2016) 110–120
[21]. S.A.A.Nami et.al/ journal of photochemistry and photobiology, B: 160 (2016) 392-399
[22]. Z. H. Chohan, M. Arif, M. A. Akhtar, and C. T. Supuran J. Bioinorganic Chemistry and Applications, vol., Article ID 83 (2006)131, 13 pages.
[23]. N. S. Korde, S. T. Gaikwad, B. C. Khade, A. S. Rajbhoj. Chem. Sci. Trans.2(2013).
[24]. Nanda S. Korde, Suresh T. Gaikwad, Seems S. Korde, Anjali S. Rajbhoj J. of Rec. Tech. and Engine; 2:4 (2013)
[25]. U. Kumar, S. Chandra J. Saudi Chem. Soc. 15(2011) 187–193.
[26]. V.K. Revankar, V.B. Mahale Indian J. Chem. A 28(1979) 683.
[27]. Satyajit D. Sarker, Lutfun Nahar, Yashodharan Kumarasamy phytochem.42,(2007)321–324
[28]. Michel F. Sanner. J. Mol. GraphicsMod. 17,(1999) 57-61.
[29]. K. Mohanan, S.N. Devi Russ. J. Coord. Chem. 32(2006)600.
[30]. P.S. Mane, S.G. Shirodkar, B.R. Arbad, T.K. Chondhekar Indian J. Chem.40(2001) 648.