Synthesis, Characterization and Microbial Evaluation of Metal Complexes of Molybdenum with Ofloxacin (Levo (*S*-form) and Dextro (*R*-form)) Isomers

Qadeer K. Panhwar[1,2] and Shahabuddin Memon[2,*]

[1]*Dr. M. A. Kazi Institute of Chemistry, University of Sindh, Jamshoro, Pakistan*

[2]*National Center of Excellence in Analytical Chemistry, University of Sindh, Jamshoro 76080, Pakistan*

Abstract: The article describes the interaction of molybdenum with dextrofloxacin and levofloxacin (isomers of ofloxacin) antibiotic drugs. Characterization of compounds was made by UV-Vis, FT–IR, ^{1}H NMR, elemental and thermogravimetric analyses. The green colored Mo–dextrofloxacin and yellow colored Mo–levofloxacin complexes were isolated. After complete characterization, the chemical formulae of the complexes were established as $[MoO_2(R\text{-Oflox})_2]$ or $[MoO_2(Dextro)_2]$ and $[MoO_2(Levo)_2]$ or $[MoO_2(S\text{-Oflox})_2]$. The microbial evaluation was made by well diffusion method for both ligands and their metal complexes against two bacterial strains, *S. aureus* and *E. coli*. It was observed that the antibacterial action of Mo–dextrofloxacin and Mo-levofloxacin was significantly higher than the dextrofloxacin and levofloxacin alone against *S. aureus*, while no action was observed against *E. coli*.

Keywords: Antibacterial, synthesis, levofloxacin, ofloxacin, molybdenum.

INTRODUCTION

In 1945, Selman A. Waksman firstly used the term ‘‘antibiotic’’ in the title of his book. He defined the term as “….produced by microorganisms and which possess the property of inhibiting the growth and even of destroying other microorganisms.” Antibiotics may be synthetic or semi–synthetic. Many antibiotics do not require metal ions to show bioactivities, however, a big number may require metal ions for proper functioning e.g. bacitracin, bleomycin (BLM), and streptonigrin (SN) [1]. The chelate formation may increase the lipophilicity of drug, which may increase the drug action because of effectual drug permeability into the site of action [2].

Quinolines are a popular collection of antibiotics used for treating several bacterial diseases. The significant growth in the quinoline drug family was observed with the discovery of nalidixic acid in 1962. Till to date, this family has been grown to almost 10 thousand analogous. Quinolines have ability to pass through cells easily and hence can be utilized for the treatment of intracellular pathogens such as Mycoplasma pneumoniae and Legionella pneumophila [3-5]. It may be proposed that uncharged quinolines may diffuse through cytoplasmic membranes, where presence of metal ion may result in higher uptake of quinolines by bacterial cells relative to only drug. Hence, metal complexes’ formation may enhance bioavailability of ligands or metal ions or both [6]. Fluoroquinolines are substituted quinolines having a fluorine atom at position 6. This fluorine atom may increase gyrase inhibition and cell penetration. Main structural importance is that its piperazinyl subtituent is active against Gram –ve bacteria while pyrrolidinyl moiety act against Gram +ve cocci. Whereas position 8 with substituted function may control anaerobe activity [4]. In addition to be broad spectrum antimicrobial agents, fluoroquinolines may also have some other useful characteristics which may increase its bioavailability, penetration into tissues, safety as well as long term serum half-life. These properties may be the basis to make them very efficient agents to treat variety of diseases such as respiratory, soft tissue, urinary tract, and bone-joint infections as well as sexually transmitted diseases, typhoid fever, community acquired pneumonia, prostatitis, sinusitis, and acute bronchitis [7, 8].

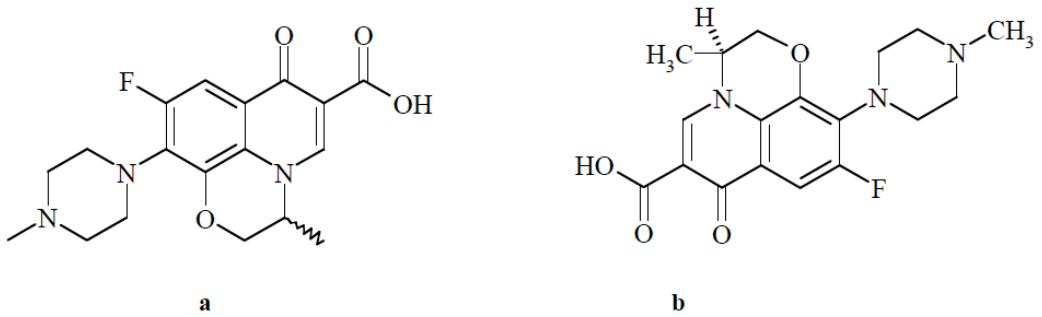
Dextrofloxacin and levofloxacin (Figure **1**) are two well–known examples of fluoroquinolines.

Racemic ofloxacin (50% Dextrofloxacin and 50% Levofloxacin) is synthetic [9] broad spectrum antibacterial agents against G (+ve) and G (–ve) bacterial strains [10, 11] and extensively exercised for clinical purpose [12]. They inhibit bacterial DNA gyrase, and hence DNA replication and transcription [11, 13, 14].

All bacteria may have an essential enzyme known as DNA gyrase and antibiotics may efficiently target it. Quinolines work against DNA gyrase and turn its action

*Address correspondence to this author at the National Center of Excellence in Analytical Chemistry, University of Sindh, Jamshoro 76080, Pakistan; Tel: +92 (22) 9213429-30; Fax: +92 (22) 9213431;
E-mail: shahabuddinmemon@yahoo.com

E-ISSN: 2308-8044/14 **© 2014 Synergy Publishers**



a **b**

Figure 1: Structures of **a**) ofloxacin (*R*-form) and **b**) levofloxacin.

against bacteria as well as block the strand passage and prevent proper DNA replication which ultimately cause cell death [15]. Ofloxacin is known as a member of second [13] and levofloxacin third generation [15]. Their structures have oxazine ring with N–1 and C–8 connected through ring structure. The same ring also contains methyl group that may exist in two optically active forms i.e., *S*–isomer and *R*–isomer. Initially, racemic ofloxacin was available as a drug but later it was replaced by active *S*–isomer (Trade name levofloxacin) isolated from the racemic ofloxacin, which is currently a leader on the quinolone drug market. Since, the *S*-isomer has significantly higher antibacterial activity almost two orders of the magnitude as compared to *R*-isomer. It is quite surprising that just a methyl group (non-functional) with respect to the plane of ring may show the different steric configurations (due to structural differences) for two enantiomers [11, 16]. Not only bicyclic heteroaromatic pharmacophore may impart the antibacterial property to the fluoroquinoline drugs, but it may also depend upon nature and the spatial arrangement of tangential substituents. Such substituents may influence the antibacterial action in order to offer more attraction to bacterial enzymes as well as increasing cell penetrations [15].

In literature, many complexes have been reported with their bioactivities such as ofloxacin complexes of Cu, Co, Mg, Zn and Ru [10], magnesium complexes of *S*-form and *R*-form [16], copper complexes of *S*-form and *R*-form [17] and Cu^{II}, Ni^{II}, Mn^{II}, and Fe^{III} complexes of levofloxacin [15].

Several drugs when administered as metal complexes may acquire modified toxicological and pharmacological properties [3]. Chemistry of drug–metal coordination compounds is more popular to design drugs of additional bioactivity. Action of many drugs is affected by metal ions that enhance the efficacy of drugs upon coordination [18]. Many transition metal complexes have been used as drugs for treating a variety of ailments and disorders as observed in research showing considerable use of such complexes against lymphomas, carcinomas, infection control, diabetes, anti–inflammatory, and neurological disorders because complexes show a great diversity in action [2]. The ability of fluoroquinolone antibiotics to interact with some cellular components is mediated by their complexation with divalent metal cations. While major structural difference between two kinds of drugs may be responsible for their mode of action or mechanism of penetration into a bacterium [19]. The formation of complexes also increases the bioavailability of metal ion or the ligand drug, or both due to increased hydrotropy and liposolubility may enhance the ability of drug molecules in crossing the membrane of a cell, and hence raised the biological utilization ratio and activity of the drug [20].

Metal coordination to biologically active molecules can be used as a strategy to enhance their activity and overcome resistance [15]. Our strategy is the synthesis and isolation of new metal complexes of levofloxacin and dextrofloxacin with Mo and characterization through ^{1}H NMR, UV–Vis, Elemental analysis, IR, conductance measurements and thermal analysis and microbial evaluation against two bacterial species, Staphylococcus aureus and Escherichia coli. Today, little articles have been reported on the coordination properties of levofloxacin [21].

EXPERIMENTAL

General Experimental Procedures

All the reagents and solvents were of analytical grade or chemically pure. Drugs were purchased from Alchemy pharmaceuticals (Pakistan), KBr from Aldrich Chemical (Germany). Sodium molybdate was purchased from Fluka (Switzerland). Acetic acid was obtained from (Spain). All the reagents were weighed within an accuracy of ± 0.0001 g.

UV–Vis spectra were obtained using a Perkin Elmer Lambda 35 (USA) UV–Vis double beam spectrophotometer, using standard 1.00 cm quartz cells. Electrolytic conductance of the complexes was measured by Inolab cond 720 WTW series conductometer. FT-IR spectra were recorded in the spectral range of 4,000–400 cm^{-1} on a Thermo Scientific Nicolet *i*S10 FT–IR (USA) instrument using KBr pellets. ^{1}H NMR spectra were recorded on a Bruker 500 MHz (Germany) spectrometer in DMSO using TMS as internal standard. Chemical shifts are given in δ relative to TMS. Thermogravimetric–differential thermal analysis (TG–DTA) curves were obtained on a Pyris™ Diamond TG–DTA (Perkin–Elmer) under a nitrogen atmosphere at a heating rate of 10 °C min^{-1} from ambient to 600 °C.

Synthesis of Metal Complexes

0.0723 g, 0.02 mmol of dextrofloxacin and 0.074 g, 0.02 mmol of levofloxacin was dissloved in 10, 10 mL of acetic acid, respectively. Subsequently, 0.0421g, 0.01 mmol of molybdenum salt was dissolved in distilled water (10 mL) and mixed metal and ligand solutions to each other. Quickly the precipitates appeared within solutions. Put aside the solutions till to settle the precipitates. Filtered the solutions, separated the precipitates and washed with distilled water. Both the products were air–dried. After complete drying, the color of precipitates was observed as yellow for Mo–levofloxacin, while initially yellow for Mo–dextrofloxacin but after complete drying it turned green. The % yield was found as 72% and 75% for Mo–dextrofloxacin and Mo–levofloxacin, respectively. The elemental analysis results obtained for $[MoO_2(R\text{-Oflox})_2]$ complex are: C, 50.82; H, 4.7; N, 9.88%, while for $[MoO_2(S\text{-Oflox})_2]$ are: C, 51.02; H, 4.15; N, 9.90%, respectively.

Antimicrobial Assay

Synthesized drug–metal complexes were applied for antibacterial assay. The assay was carried out using well diffusion method against two bacterial strains i.e., *S. aureus* (Gram +ve) ATCC 25923 and *E. coli* (Gram –ve) ATCC 25922. The analysis was carried out at a fixed concentration of 20 µg/mL. The solvent DMSO was used as a –ve control. The medium of Muller Hunton Agar was used for said species.

RESULTS AND DISCUSSION

Complexes were formed by usual complex formation methods. Both the metal–complexes were colored. The complexes were characterized and their formulae and structure was determined by elemental analyses, molar conductivities, FT-IR data, thermal analysis, ^{1}H NMR spectra. From the data of elemental analysis and molar conductivity, $[MoO_2(Oflox)_2]$ and $[MoO_2(Levo)_2]$ were judged as non–electrolytes with values 4.8 and 3.99 µS/cm in DMSO, respectively, and thus their general chemical formulae were estimated as$[M(L)_2]$. From spectral analysis like FT-IR and ^{1}H NMR, we could be in position to identify the ligation sites in the drug ligands. Besides, experimental data fitted well with the calculated formula, there was no crystallization water molecules in the complexes, as checked by thermal analysis well as FT-IR. Both complexes have been prepared in high yield (72–75%) *via* the addition of acetic acid solution of ofloxacin (*R*-form) and levofloxacin to an aqueous solution of the metal ion at a ratio 2:1 according to the reactions (1) and (2):

$$Na_2MoO_4 + 2CH_3COOH \rightarrow 2NaCH_3COO + H_2O + MoO_3 \quad (1)$$

$$MoO_3 + 2Oflox \rightarrow MoO_2(Oflox)_2 + H_2O \text{ or} \quad (2)$$

$$MoO_2^{2+} + 2Oflox^- \rightarrow MoO_2(Oflox)_2$$

Both the resultant complexes are soluble mainly in hot DMSO, DMF, ethanol and methanol, while insoluble in all the other solvents.

The close proximity of keto and carboxyl groups on levofloxacin and ofloxacin (*R*-form) may impart good chelating properties to both molecules. Hence, electronic spectra were carried out to characterize their metal complexes, in MeOH. Their spectra were almost similar to drug molecules with negligible bathochromic shift and ligands retain their structures in complexes. Since bands in metal complexes are observed at similar regions because of possessing similar chromophores. UV bands in 260–340 nm region may be caused by π–π* intraligand transitions. Strong absorption at lower wavelength may be caused by chromophore. The strong absorption peak corresponds to the chromophore related to nitrogen of position 1 to carboxyl group, while weak one may arise from chromophore of nitrogen from piperazinyl group at 7–carbon to keto group. No any absorption band is seen in visible region even using higher sample concentrations. In previous literature, no d–d bands are observed for such complexes except few ones. Whereas, using solid–state diffuse reflectance, d–d bands are observed for ofloxacin complexes [7].

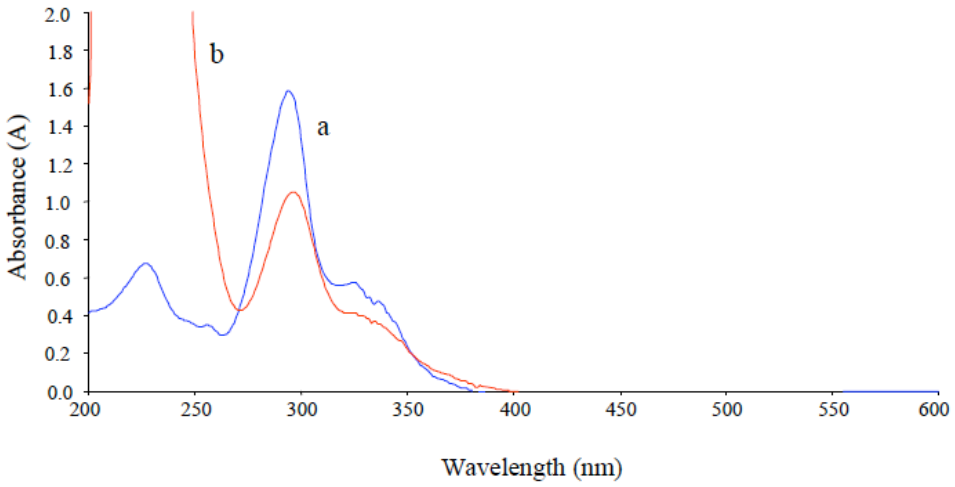


Figure 2: Electronic spectra of **a**) Ofloxacin (*R*-form) and **b**) Mo–complex in MeOH, bands in ofloxacin (*R*-form) = 227 nm, 294 nm, 325 nm, and in Mo–complex = 297 nm, 326 nm.

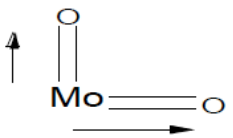
In present case, ofloxacin (*R*-form) shows two maxima at 227, 294 nm, and a shoulder at 325 nm in UV region, while in its molybdenum complex studied in methanol shows negligible shift to 297 and 326 nm (Figure **2**), respectively. These both are intraligand transitions because they have just shifted little and no any new peak was formed. Thus, the spectrum is affected when ofloxacin form complexes with metallic cation MoO_2^{2+} leading to a red shift of the strong absorption peak to 297 nm. UV spectra of the complexes are practically identical with that of the ofloxacin (*R*-form) and levofloxacin ligands but just slightly shifted, indicative of coordination through the pyridone oxygen and one carboxylate oxygen [22]. As expected, these complexes are diamagnetic in nature. No d–d transitions are observed for these complexes consistent with d^0 configuration.

The complexes of levofloxacin and ofloxacin (*R*-form) characterized by FT-IR show obvious changes in their spectra relative to complexes.

Levofloxacin and Mo–Levofloxacin Complex

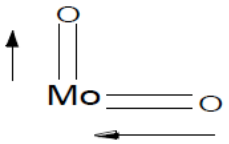
Metal carboxylates show a very strong band due to carboxylic C=O, which may be replaced by two peaks generated from asymmetrical and symmetrical stretchings of COO^- group. Because both C–O groups show equal bond orders for carboxylate ion caused by electron delocalization. Since, degree of interaction between metal centre and coordinated carboxylate group may affect delocalization as a result stretching frequencies of carboxylate ions as well [23]. Levofloxacin shows two characteristic absorption peaks at 1719 and 1623 cm^{-1} for C=O of carboxylic acid oxygen and keto oxygen of levofloxacin ring, respectively. After complex formation, peak at 1719 cm^{-1} disappeared by showing that carboxyl group has been involved in complex formation, while peak at 1623 shifted to lower value of wave number 1583 cm^{-1} (Figure **3**). These variations may suggest that levofloxacin is coordinated to molybdenum *via* pyridone oxygen and one carboxylate oxygen [24].

Nakamoto and his co–workers suggested that in carboxylate ion the difference of asymmetric and symmetric stretching vibrations ($\Delta\nu_{COO}$–) may be used to indicate its coordination/bong mode [25]. The separation Δν ($\nu_{asymm}(CO_2)$–$\nu_{sym}(CO_2)$) of 176–257 cm^{-1} range may specify the mode of monodentate coordination for carboxylate moiety [26]. Thus, disappearance of peak at 1719 cm^{-1} in levfloxacin may give rise to two strong peaks at 1584 cm^{-1} and 1408 cm^{-1} in Mo–levofloxacin complex, with difference of 176 cm^{-1} indicating monodentate coordination mode of carboxylate ion.



symmetric stretch

ν_{sym}



asymmetric strectch

ν_{asym}

The dioxomolybdenum(VI) complex of levofloxacin shows two absorptions for ν(Mo=O) indicating *cis* arrangement of two oxygen atoms around Mo atom [27] for $\nu_{asym}(MoO_2)$ and $\nu_{sym}(MoO_2)$ stretches to confirm the formation of mononuclear complex [28] with a *cis*–$[MoO_2]^{2+}$ core [29]. Thus, dioxomolybdenum(VI) prefers to form complex of *cis* arrangement by maximum utilization of d–orbital or dπ groups for

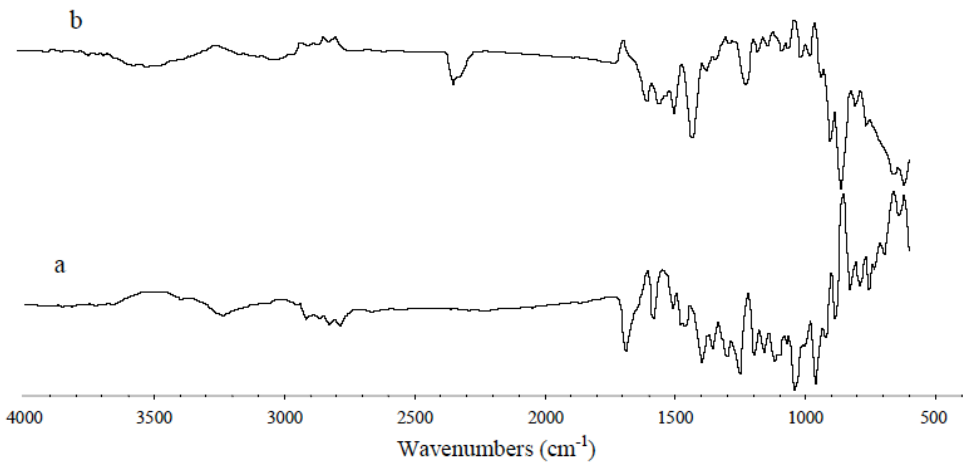


Figure 3: IR spectra of **a**) Levofloxacin and **b**) Mo–levofloxacin complex.

bonding [30]. The *cis* arrangement in Mo-levofloxacin may be characterized by two IR bands at 941 and 902 cm^{-1} for v_{asym}(O=Mo=O) and v_{sym}(O=Mo=O) in C_{2V} symmetry, respectively [31]. The *trans*–MoO_2^{2+} may give rise single strong IR active peak for v_{as}(O=Mo=O) [32] but this configuration is rarely exhibited by metal dioxo complexes. The peaks at 703 and 665 cm^{-1} may be attributed to Mo–O bonds for metal and ring oxygens.

Ofloxacin (*R-form*) and its Molybdenum Complex

After comparing IR absorptions of ofloxacin (*R*-form) with its molybdenum complex, these main conclusions were obtained: (1) ofloxacin (*R*-form) shows two strong absorption peaks at 1710 cm^{-1} for $v(C=O)_c$ and 1618 cm^{-1} $v(C=O)_p$; (2) the carboxylic band shifted to 1701 cm^{-1} in complex spectrum shows the involvement of this moity in complexation (3) In addition, techniques show no definite conclusion regarding the involvement of ketone group in complex formation. Band at 1618 cm^{-1} in ofloxacin (*R*-form) ligand molecule may appear at 1626 cm^{-1} is either due to carboxyl or ketone group for bonding metal ion [3]. However, suggested changes in the spectrum of complex relative to ofloxacin (*R*-form) alone may recommend the coordination of ofloxacin (*R*-form) with metal ion through carboxylate and pyridone oxygens. There two strong absorption bands for *cis* arrangement of MoO_2^{2+} may arise at 904 and 940 cm^{-1} for symmetricl and symmetrical vibration [27] resulting from the *cis*–dioxo Mo cores [33].

The ^{1}H NMR study was carried out to support the coordination of molybdenum to both ligands ofloxacin (*R*-form) and levofloxacin. But, it was observed that only one major change is observed in the spectra of complexes relative to their ligands. That change was for carboxylic proton. In both complexes signal of carboxylic proton is vanished, which is present in both the ligands before complexation in ofloxacin (*R*-form) at 11.27 ppm and in levofloxacin at 11.15 ppm. But these signals are absent in molybdenum complexes [21]. Whereas, aryl protons appeared downfield in complexes. In case of levofloxacin complex, there is downfield shift of aryl protons i.e. from 8.05 to 8.27 for 2H, and 7.51 to 7.75 ppm for 5H. While for ofloxacin (*R*-form) it is 9.25 to 9.59 and 7.70 to 7.97 ppm, respectively [15]. The negligible shift of hardly 0.2 to 0.3 ppm is taking place in aryl protons [34] perhaps either due to coordination causing change in configuration of complexes as compared to ligands. It also indicated that coordination has changed the magnetic environment of aromatic ring protons [35].

The piperazine and aliphatic protons remain almost unchanged. It is because these protons are lying significantly far from the coordination sites in both ligands. Hence, they are not affected at all. It suggested that –COOH group is involved in coordination with metal ion by replacement of its proton. Hence coordination takes place in molybdenum and drug ligands *via* vicinal carbonyl and carboxyl groups. Because almost all the signals observed in ligand protons are present in complexes at same place as in ligand drug molecules expect disappearance of carboxylic protons [36]. Thus, it supports the results obtained from FT-IR spectroscopy that metal ions coordinates to drug molecules through carboxylic and pyridone oxygen atoms. The structure of molybdenum complexes of ofloxacin (*R*-form) and levofloxacin is given in Figure **4**.

The thermal analysis (TG, DTA) was performed in order to establish the thermal stability of these

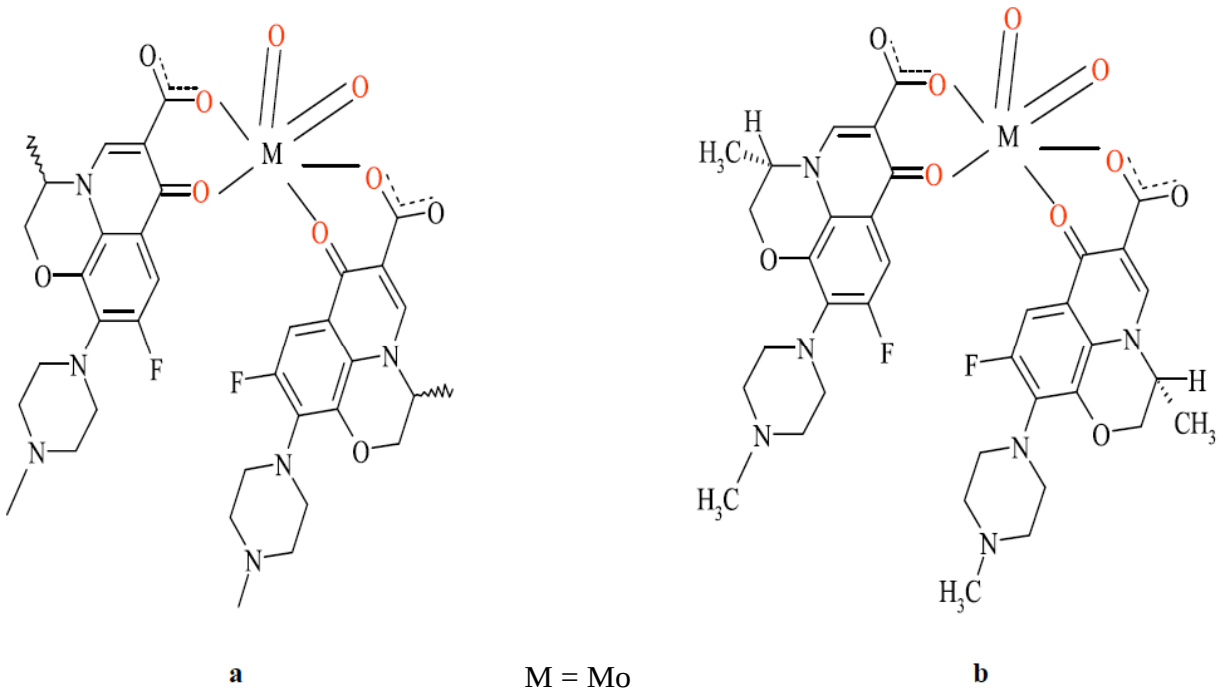


Figure 4: Chemical Structures of **a**) $[MoO_2(R\text{-Oflox})_2]$ and **b**) $[MoO_2(Levo)_2]$ complexes.

complexes during the pharmaceutical development studies.

Mo–Ofloxacin

In the case of Mo–ofloxacin (Figure **5**), the first stage shows slow weight loss between ambient to 260 ºC due to the loss of moisture/residual solvents, but the TG trace in this region also reflects the decreased rate at which solvent molecules undergo loss. This may probably be due to the trapping of solvent molecules in the molecular network of the ofloxacin (*R*-form). The trace also shows two subsequent small weight losses of the magnitude less than 6% between 260 to 300 ºC. This stage is onset of decomposition and it is likely that complex at this stage suffers from loss of some species in its structure. It is likely that some part of the bulky ligand molecule is lost at this stage. The third weight loss occurs between the 350 to 550 ºC being approximately equal to 36.5%. This part of curve reflects slow loss showing no apparent signs of decomposition. The bulky molecule in this region shows good stability and volatility (that does not break move as a whole). During this stage weight loss and volatalisation of degradation product take place rapidly. Beyond, 400°C the weight loss is about 6–7%. DTA shows that it undergoes glass transition, shows melting endotherm, undergoes decomposition and finally volatilization endotherm accompanied by swelling of bulky organic molecule. DTG shows at first the

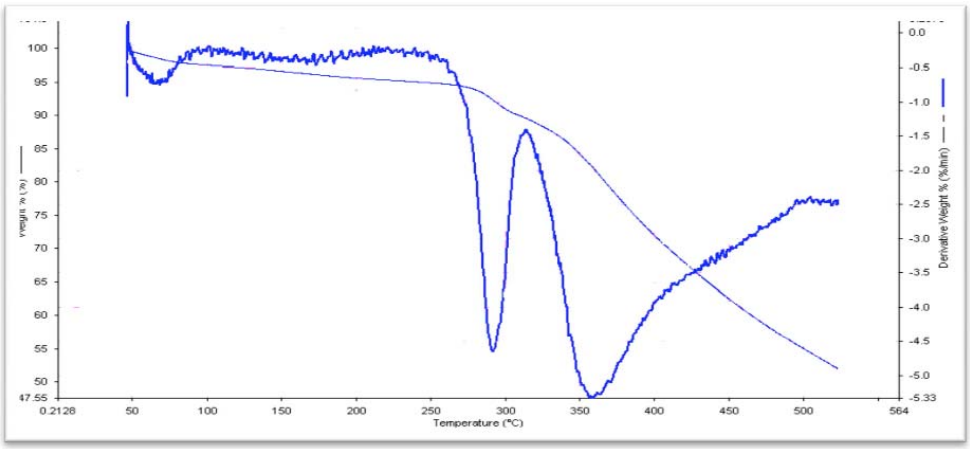


Figure 5: TG–DTG of Mo–Ofloxacin (*R*-form) complex.

moisture/solvent, then for 1st break T_i at 260, T_{max} at 290, T_f at 360 ºC, for 2nd break T_i at 265, T_{max} at 355, and T_f at 510 º C. However, there is a continuous decomposition upto 565 ºC.

Mo–Levofloxacin

In the case of Mo–levofloxacin, this shows the thermal events similar to ofloxacin (*R*-form) complex, but there is difference of temperatures in both of the endothermic traces. It has degree of glass transition different as well as slow melting along with slow weight loss.

The antibacterial activity of drug molecules and their respective complexes was carried out. From the results, it was observed that the antibacterial action of all the compounds was higher against *s. aureus* (Figure **6**) relative to *E. Coli* and the antibacterial action of both the complexes is higher than their corresponding ligands. While the activity of levofloxacin is higher than ofloxacin (*R*-form). Because former is known to a very effective antibacterial agent. Similarly the molybdenum complex of levofloxacin has higher activity than ofloxacin (*R*-form) complex.

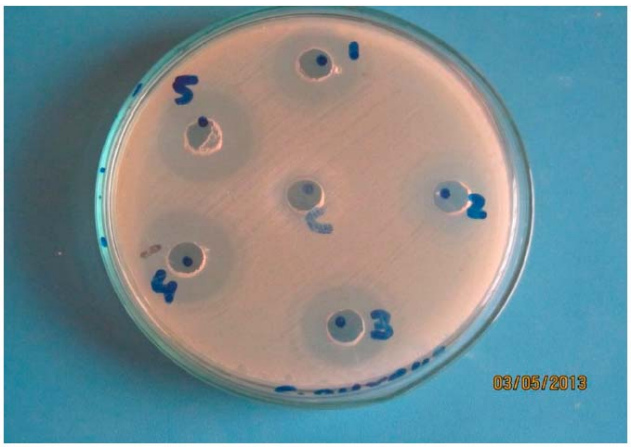


Figure 6: Relative inhibitory action of 2) Mo–ofloxacin (*R*-form), 3) ofloxacin (*R*-form), 4) Mo–levofloxacin, 5) levofloxacin, and c) control (DMSO) against *S. aureus* in Muller Hunton Agar medium.

The metal complex showing better antimicrobial activity than the parent drug may have potential to be used as antibacterial and must be explored further [18]. Thus, levofloxacin and its complex have more inhibitory action relative to ofloxacin (*R*-form) and its Mo complex. It shows that antibacterial activity of metal complex is higher than uncomplexed ligand. Anyway, increased antibacterial action of metal chelate of Mo–levofloxacin relative to uncomplexed drug ligand can be explicated on the basis of metal's oxidation state, overtone concept and Tweedy's chelation theory. Overtone concept of cell permeability states that antibacterial action is controlled by liposolubility because from lipid membrane (surrounding cells) only lipid soluble materials are allowed to pass through it. Chelation/complexation greatly reduces the metal ion's polarity because ligand orbitals may overlap and may partly share the +ve charge of metal ion with donor groups. That causes to increase the delecalization of π/n–electrons over the chelate ring as a whole and lipophilicity of complexes/coordination compounds may increase. Hence higher lipophilicity may increase the penetration of complexes through lipid membranes and thus in microorganisms metal binding sites in enzymes are blocked. The respiration process of cell has also been disturbed by the complexes that cause the blockage of protein synthesis that inhibits the more growth of organisms [37]. Difference in antibacterial activity of various complexes against various microorganisms may either depend upon cells impermeability of microbes or ribosomal differences of microbial cells. Table **1** indicates the antibacterial activities results.

Table 1: Zone of Inhibition (mm) of Ofloxacin (*R*-form) and Levofloxacin and their Molybdenum Metal Complexes against a Gram +ve and Gram –ve Bacterial Cultures

Compounds	Concentration	Bacterial species	
		S. aureus	***E. coli***
Ofloxacin (*R*-form)	20 µg mL^{-1}	19	17
Mo-Ofloxacin	20 µg mL^{-1}	22	17
Levofloxacin	20 µg mL^{-1}	21	18
Mo-Levofloxacin	20 µg mL^{-1}	23	18
Control (DMSO)	-	0	0

In the case of *E.coli*, the antibacterial action of both the ligands is comparable with their complexes. In general, position as well as nature of substituents attached to phenyl rings is decisive for their antimicrobial activities. Hence, the lesser antibacterial activities of complexes may account for their lower lipid solubility. Thus, it is difficult for metal ion to reach at desirable site of action for interfering normal activity of cell. Since, nature of metal ion has key role to determine the antimicrobial activities [38].

CONCLUSIONS

It has been concluded from the study that a complex of suitable geometry was formed between

molybdenum and ofloxacin (*R*-form and *S*-form) drug molecules. The resulting complexes were characterized by different analytical techniques such as UV-Vis, FT-IR and ^{1}H NMR. From the data obtained through these techniques, the molecular formula of the complexes was established as $MoO_2(L)_2$, which is consistent with obtained results. The dioxomolybdenum complexes were of *cis* configuration in both cases, where the metal ion was coordinated *via* carboxylate and pyridone oxygens in both cases. Antibacterial results demonstrated that molybdenum complexes of ofloxacin (*R*-form and *S*-form) were more active than uncomplexed drug against *S. Aureus*, but they do not show any effect against *E. Coli*.

ACKNOWLEDGEMENTS

We are thankful to National Centre of Excellence in Analytical Chemistry, Department of Microbiology, and Institute of Advanced Studies and Research, University of Sindh, Jamshoro/Pakistan for providing necessary facilities to complete this work.

REFERENCES

[1] Ming L-J. Structure and function of “metalloantibiotics”. Med Res Rev 2003; 23: 697-762. http://dx.doi.org/10.1002/med.10052

[2] Sabale PM, Kaur P, Patel Y, Patel J, Patel R. Metalloantibiotics in therapy: an overview. J Chem Pharm Res 2012; 4: 4921-36.

[3] Wu G, Wang G, Fu X, Zhu L. Synthesis, crystal structure, stacking effect and antibacterial studies of a novel quaternary copper (II) complex with quinolone. Molecules 2003; 8: 287-96. http://dx.doi.org/10.3390/80200287

[4] Sadeek SA, El-Shwiniy WH. Metal complexes of the third generation quinolone antibacterial drug sparfloxacin: preparation, structure, and microbial evaluation. J Coord Chem 2010; 63: 3471-82. http://dx.doi.org/10.1080/00958972.2010.514049

[5] Imran M, Iqbal J, Iqbal S, Ijaz N. *In vitro* antibacterial studies of ciprofloxacin–imines and their complexes with Cu(II),Ni(II),Co(II), and Zn(II). Turk J Biol 2007; 31: 67–72.

[6] Shaikh AR, Giridhar R, Megraud F, Yadav MR. Metalloantibiotics: synthesis, characterization and antimicrobial evaluation of bismuth–fluoroquinolone complexes against Helicobacter pylori. Acta Pharm 2009; 59: 259-71. http://dx.doi.org/10.2478/v10007-009-0027-6

[7] Obaleye JA, Akinremi CA, Balogun EA, Adebayo JO, Omotow AB. Synthesis, characterisation, antimicrobial and toxicological studies of some metal complexes of norfloxacin and ofloxacin. Centrepoint (Science Edition) 2009; 16: 37-56.

[8] Turel I. The interactions of metal ions with quinolone antibacterial agents. Coord Chem Rev 2002; 232: 27-47. http://dx.doi.org/10.1016/S0010-8545(02)00027-9

[9] Okeri HA, Arhewoh IM. Analytical profile of the fluoroquinolone antibacterials. I. Ofloxacin. Afri J Biotech 2008; 7: 670-80.

[10] Živec P, Perdih F, Turel I, Giester G, Psomas G. Different types of copper complexes with the quinolone antimicrobial drugs ofloxacin and norfloxacin: structure, DNA– and albumin–binding. J Inorg Biochem 2012; 117: 35-47. http://dx.doi.org/10.1016/j.jinorgbio.2012.08.008

[11] Mohd A, Khan AAP, Bano S, Siddiqi KS. Interaction and fluorescence quenching study of levofloxacin with divalent toxic metal ions. Eurasian J Anal Chem 2010; 5: 177-86.

[12] Azcurra AI, Yudi LM, Baruzzi AM, Kakiuchi T. Interfacial behavior of ofloxacin–Fe(III) complex at the water /1,2–dichloroethane interface: a voltfluorometric and chronofluorometric study. J Electroanal Chem 2001; 506: 138-42. http://dx.doi.org/10.1016/S0022-0728(01)00493-4

[13] De PK, Sahana B, Rakshit S. Enhancement of dissolution rate and stability study of ofloxacin solid dispersion. Der Pharmacia Sinica 2011; 2: 169-81.

[14] Macıas B, Villa MV, Rubio I, Castineiras A, Borras J. Complexes of Ni(II) and Cu(II) with ofloxacin Crystal structure of a new Cu(II) ofloxacin complex. J Inorg Biochem 2001; 84: 163-70. http://dx.doi.org/10.1016/S0162-0134(01)00182-9

[15] Sultana N, Arayne MS, Rizvi SBS, Haroon U, Mesaik MA. Synthesis, spectroscopic, and biological evaluation of some levofloxacin metal complexes. Med Chem Res 2013; 22: 1371-7. http://dx.doi.org/10.1007/s00044-012-0132-9

[16] Drevensek P, Kosmrlj J, Giester G, *et al*. X–Ray crystallographic, NMR and antimicrobial activity studies of magnesium complexes of fluoroquinolones–racemic ofloxacin and its S–form, levofloxacin. J Inorg Biochem 2006; 100: 1755-63. http://dx.doi.org/10.1016/j.jinorgbio.2006.06.011

[17] Li Y, Chai Y, Yuan R, Liang W. Synthesis and application of a new copper(II) complex containing oflx and leof. Russ J Inorg Chem 2008; 53: 704-6. http://dx.doi.org/10.1134/S0036023608050070

[18] Akinremi CA, Obaleye JA, Amolegbe SA, Adediji JF, Bamigboye MO. Biological activities of some fluoroquinolones–metal complexes. Int J Med Biomed Res 2012; 1: 24-34. http://dx.doi.org/10.14194/ijmbr.115

[19] Park H-R, Oh C-H, Lee H-C, Choi JG, Jung B-I, Bark K-M. Quenching of ofloxacin and flumequine fluorescence by divalent transition metal cations. Bull Korean Chem Soc 2006; 27: 2002-10. http://dx.doi.org/10.5012/bkcs.2006.27.12.2002

[20] Chen C, Chen K, Long Q, Ma M, Ding F. Structural characterization and DNA–binding properties of Sm(III) complex with ofloxacin using spectroscopic methods. Spectroscopy 2009; 23: 103-11. http://dx.doi.org/10.1155/2009/769146

[21] Chen C-Y, Chen Q-Z, Wang X-F, Liu M-S, Chen Y-F. Synthesis, characterization, DNA binding properties, and biological activities of a mixed ligand copper(II) complex of ofloxacin. Trans Met Chem 2009; 34: 757-63. http://dx.doi.org/10.1007/s11243-009-9259-z

[22] Park H-R, Oh C-H, Lee H-C, Choi JG, Jung B-I, Bark K-M. Quenching of ofloxacin and flumequine fluorescence by divalent transition metal cations. Bull Korean Chem Soc 2006; 27: 2002-10. http://dx.doi.org/10.5012/bkcs.2006.27.12.2002

[23] Lewis J, Wilkins RG. Modern coordination chemistry, Interscience Publishers, New York 1960.

[24] El-Shwiniy WH, El-Attar MS, Sadeek SA. Metal Complexes of enrofloxacin part I: preparation, spectroscopic, thermal analyses studies and antimicrobial evaluation. J Korean Chem Soc 2013; 57: 52-62. http://dx.doi.org/10.5012/jkcs.2013.57.1.52

[25] Nakamoto K. Infrared and Raman Spectra of Inorganic and Coordination Compounds, Wiley, New York 1978.

[26] Manimekalai R, Kalpanadevi K, Sinduja CR. Coordination aspects of newly synthesized complexes of some divalent transition metals with 2,4-dichlorophenoxy acetate and hydrazine. Chem Sci Trans 2013. http://dx.doi.org/10.7598/cst2013.406

[27] Psomas G. Mononuclear metal complexes with ciprofloxacin: Synthesis, characterization and DNA-binding properties. J Inorg Biochem 2008; 102: 1798-811. http://dx.doi.org/10.1016/j.jinorgbio.2008.05.012

[28] Gusina L, Bulhac I, Dragancea D, Simonov YA, Shova S. Structural and spectroscopic characterization of dioxomolybdenum(VI) complexes with schiff bases derived from isonicotinoylhydrazide. Rev Roum Chim 2011; 56: 981-5.

[29] Sovilj SP, Mitić D, Drakulić BJ, Milenković M. Spectroscopic properties and antimicrobial activity of dioxomolybdenum(VI) complexes with heterocyclic S,S'-ligands. J Serb Chem Soc 2012; 77: 53-66. http://dx.doi.org/10.2298/JSC110328160S

[30] Patil SK, Naik VM, Mallur NB. Synthesis, spectral and antibacterial studies of oxomolybdenum (V) and dioxomolybdenum (VI) complexes with 2–imidazolyl mercaptoaceto hydrazone. Der Pharma Chemica 2012; 4: 1812-8.

[31] Rao DP, Yadav HS, Yadava AK, Singh S, Yadav US. Synthesis and characterization of cis–dioxomolybdenum(VI) complexes having furil as a precursor molecule. J Serb Chem Soc 2012; 77: 1205-10. http://dx.doi.org/10.2298/JSC111110020R

[32] Maurya RC, Sutradhar D, Sahu S, Bohre P. Synthesis, characterization and 3d molecular modeling of some new 8–coordinate cis–dioxomolybdenum vi) chelates involving (o, n, o)–donor coordination matrix of schiff bases derived from 4–amino–2,3–dimethyl–1–phenyl–2–pyrazolin–5–one and some β–diketoenolates. Rasayan J Chem 2008; 1: 395-412.

[33] Zhou Z–H, Wang H, Yu P, Olmstead MM, Cramer SP. Structure and spectroscopy of a bidentate bis–homocitrate dioxo–molybdenum(VI) complex: Insights relevant to the structure and properties of the FeMo–cofactor in nitrogenase. J Inorg Biochem 2013; 118: 100-6. http://dx.doi.org/10.1016/j.jinorgbio.2012.10.001

[34] Vieira LMM, de Almeida MV, Lourenço MCS, Bezerra FAFM, Fontes APS. Synthesis and antitubercular activity of palladium and platinum complexes with fluoroquinolones. European J Med Chem 2009; 44: 4107-11. http://dx.doi.org/10.1016/j.ejmech.2009.05.001

[35] Sadeek SA, El–Shwiniy WH. Preparation, structure and microbial evaluation of metal complexes of the second generation quinolone antibacterial drug lomefloxacin. J Mol Struct 2010; 981: 130-8. http://dx.doi.org/10.1016/j.molstruc.2010.07.041

[36] Sadeek SA, El–Shwiniy WH. Metal complexes of the fourth generation quinolone antimicrobial drug gatifloxacin: Synthesis, structure and biological evaluation. J Mol Struct 2010; 977: 243-53. http://dx.doi.org/10.1016/j.molstruc.2010.05.041

[37] Sadeek SA, El–Shwiniy WH, Zordok WA, El-Didamony AM. Synthesis, spectroscopic, thermal and biological activity investigation of new Y(III) and Pd(II) Norfloxacin complexes. J Argent Chem Soc 2009; 97: 128-48.

[38] Joseph NRJ, Sakthivel A, Jeyamurugan R. Synthesis, structural characterization and antimicrobial studies of novel schiff base copper(II) complexes. J Chil Chem Soc 2009; 54: 354-7.

Received on 24-10-2013 Accepted on 11-01-2014 Published on 06-03-2014

DOI: http://dx.doi.org/10.12970/2308-8044.2014.02.01.1

© 2014 Panhwar and Memon; Licensee Synergy Publishers.
This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.