

RESEARCH ARTICLE

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITIES OF BIOINORGANIC COMPLEXES OF MOXIFLOXACIN.

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Abstract

Background: The growth of different organisms is controlled by drugmetal complexes which are injurious to humans. Moxifloxacin is one of the fourth generation fluoroquinolone antibiotics which inhibits DNA gyrase (a type II topoisomerase and topoisomerase IV). A number of studies were conducted on the Moxifloxacin-metal complexes regarding their biological applications. In this study synthesis and characterization of three moxifloxacin- biometal complexes with Zn(I), Ni(VI) and Co(VIII) was done and their antibacterial and antioxidant effects were studied.

Methods: Moxifloxacin- zinc chloride, nickel chloride and cobalt chloride were synthesized by mixing solutions of zinc chloride, nickel chloride and cobalt chloride with the ethanolic solution of Moxifloxacin. These metal complexes were characterized by physiochemical techniques such as FTIR, 1 H- NMR, and UV-Vis. To study the antibacterial effects of Moxifloxacin-metal complexes agar well diffusion method was used. Antioxidant activity was determined by DPPH free radical scavenging method.

Results: The structural assessment of these complexes has been carried out based on physio- chemical and spectroscopic methods. The FTIR spectra and 1H NMR clearly showed that metal-moxifloxacin complexes are formed due to change in their carboxyl stretching band in IR, H-2 and H-5 peak position in 1H NMR. Further, Zn(I), Ni(VI) and Co(VIII), moxifloxacin metal complexes have shown significant antibacterial activity against gram-positive and gram-negative bacteria. **Conclusions:** The spectral and analytical results clearly confirmed the coordination chemistry of Zn(I), Ni(VI) and Co(VIII). The moxifloxacin–Ni(VI) and Co(VIII) metal complexes showed high

moxifloxacin–Ni(VI) and Co(VIII) metal complexes showed high antibacterial activity compared to moxifloxacin--Zn(I). The antibacterial activity indicates that metal complexes have higher biological activity than parent drug (moxifloxacin).

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Introduction:-

The rapid emergence of resistant bacteria is occurring worldwide, endangering the efficacy of antibiotics, which have transformed medicine and saved millions of lives. Many decades after the first patients were treated with antibiotics, bacterial infections have again become a threat. The antibiotic resistance crisis has been attributed to the overuse and misuse of these medications, as well as a lack of new drug development by the pharmaceutical industry due to reduced economic incentives and challenging regulatory requirements.(Blair *et al.*, 2015; Ventola, 2015) In the past decades, only few new antibiotic classes (tigecycline from group of lipopeptides and tedizolid from group of oxazolidinones) have been developed and approved by FDA both of which provide coverage against Grampositive bacteria (Luepke *et al.*, 2017) Gatifloxacin, moxifloxacin and Gemifloxacin became available for general use in 2004. (Andriole, 2005).

Moxifloxacin (MOX) is a fourth generation fluoroquinolone. It is chemically is [1cyclopropyl-7-(S,S)-2,8-diazabicyclo(4.3.0)-non-8yl-6-fluoro-8-methoxy-1,4-dihydro-4-oxo-3quinoline carboxylic acid hydrochloride] (Kondaiah et al., 2017). Other Fluoroquinolones are classified into 4 generations nalidixic acid and cinoxacin (first generation), ofloxacin (OFX), norfloxacin, lomifloxacin and ciprofloxacin (CFX) (second generation), levofloxacin (LFX) (third generation) and gemifloxacin (GFX) (fourth generation). (Demir *et al.*, 2017)

Escalating resistance to moxifloxacin is being reported for many microorganisms, (Luepke *et al.*, 2017; Murray *et al.*, 2017) to overcome such resistance there are two ways, first to synthesis new antibiotics and second to prepare new drug delivery system. For synthesis of new antibiotic an average time required is ten years and at least 10 million dollars of money which is expensive and time consuming process (Fernandes & Martens, 2017).So generally the preparation of new drug delivery system of existing antibiotics is more appropriate to avoid the problem. (Kondaiah *et al.*, 2017; Skuredina, Le-Deygen *et al.*, 2017). There are 2 types of complexation methods organic (Skuredina *et al.*, 2017) and inorganic (Cuprys *et al.*, 2018; Refaat *et al.*, 2016) but the inorganic or metal complexation is more easy and less both time and money consuming then organic complexation.(Ali *et al.*, 2017; Elshafie *et al.*, 2019)

The researchers have sufficient knowledge regarding the synthesis of moxifloxacin-metal complex. The biological activities and spectral studies of moxifloxacin is reported previously by W.F. El-Hawary *et al.* On other hand the synthesis, characterization and biological activities against *E.coli*, *S. aureus*, *B. subtilis*, *Br.otitidis*, *P. aeruginosa* of the moxifloxacin-metal complexes (Ti, Y, Pd and Ce) are reported in detail.(Sadeek *et al.*, 2011). Studies on the synthesis, characterization and biological activities of moxifloxacin-imidazole-metal complexes is previously been done (Soayed *et al.*, 2013). A number of researchers have studies on the synthesis, characterization and biological activities of the moxifloxacin-metal complexes. (Nakamoto & McCarthy, 1968; Soayed *et al.*, 2013). However, the above discussed literature has not enough investigations and characterization of the moxifloxacin-metal complexes.

Moxifloxacin-metal complexes show good activity against both gram-negative and gram-positive bacteria. Fewer studies have been done with few metals complexed with moxifloxacin and very little biological activities are done on them. The synthesis of moxifloxacin-metal complexes with novel metals gave good result regarding their biological activities (Rafique *et al.*, 2010) It is the inorganic chemistry which provides a good chance to use novel metal along with other transition metals to complex with drug and give greater biological activities. (E. Maftei *et al.*, 2016; Mihorianu *et al.*, 2016) We here report the synthesis and characterization of some novel and transition metal-moxifloxacin complexes including moxifloxacin–Zn(I), Ni(VI), and Cu(VII), [Zn(MOX)₂], [Ni(MOX)₂] and [Co(MOX)₂]. Characterization was done by FTIR, H1-NMR and UV-Vis. The antibacterial activity was determined by agar well diffusion method and antioxidant activities were performed by DPPH method.

Materials and Methods: -

Drug (Moxifloxacin) and metals (Zn, Ni, and Co) were purchased from the Sigma-Aldrich Limited. The reagents and chemicals were of analytical reagent grade and were used without further purification. All magnetic stir bars and glassware were washed with double distilled water.

Synthesis of drug-metal complexation

The Moxifloxacin (1 mMole) and metal ions (0.5 mMole) were dissolved separately in methanol. The solutions were mixed and refluxed for 8 -12 hours at 60° C with continuous stirring. The resultant product was concentrated by evaporation and was precipitated using chilled chloroform. The precipitates were recrystalized.

Moxifloxacin HNMR, FTIR and U.V/VIS:

1H NMR (D₂O) ppm: δ 8.57 (s, 1H; H—2, -CH), 6.89 (d, 1H, H—5, -CH, J=13.8), 4.67 (s, 2H, H–15, -CH2), 4.06 (m, 2H, H–13, N–CH2), δ 3.91 (d, H, H-14', -CH, J=4.2), 3.70 (m, 3H, H-10 & 10', CH-CH2), δ 3.50 (s, 3H, OCH3), δ 2.76 (d, 1H, --NH–, J= 3.3), 1.88 (t, 4H, H-11 & H-12, -CH2–CH2--), δ 1.22 (q, 1H, cyclopropane, – CH), 1.09 (m, 2H, cyclopropane, CH2), 0.91 (q, 2H, cyclopropane, -CH).

IR (KBr, cm-1): 3530 (O-H stretching of COOH), 3156 (aromatic C-H stretching), 2978, 2800 (aliphatic C-H stretchings), 1709 (C=O stretching; COOH), 1620 (N-H bending), 1592, 1533 (aromatic C-C stretching), 1490 (C=C stretching), 1422, 1323 (aliphatic C-H bending), 1245 (C-F stretching), 1184 (C-O stretching), 1166 (C-N stretching), 1111 (C-C stretching), 1016, 991 (C-H bending; phenyl).

U.V/VIS (nm. 190.00 to 500.00): 195, 292, 332.

Moxifloxacin-Zinc HNMR, FTIR and U.V/VIS:

1H NMR (D₂O) ppm: δ 8.78 (s, 1H; H—2, -CH), 7.48 (d, 1H, H—5, -CH, J= 13.8), 4.07 (m, 2H, H–15, N–CH2), δ 3.88 (s, 1H, H–14',-CH) 3.77 (t, 2H, H-13, –CH2), δ 3.5 (s, 3H, –OCH3), δ 3.3 (t, 2H,H–10,N–CH2), δ 2.97 (t, 1H, H–10',N–CH–), δ 2.76 (s, 1H, --NH–,), 1.87 (q, 4H, H-11 & H-12, –CH2–CH2--), 1.09 (d, 4H, cyclopropane, CH2–CH2, J= 47.1), 0.86 (s, cyclopropane, –CH).

IR (KBr, cm-1): 3420 (O–H stretching of HOH; COOH), 3020 (aromatic C–H stretching), 2820 (aliphatic C–H stretchings), 1700 (C=O stretching; COOH), 1605 (N–H bending), 1510 (aromatic C–C stretching), 1440, 1460 (C=C stretching), 1310, 1345 (aliphatic C–H bending), 1220, 1270 (C–F stretching), 1190 (C–O stretching), 1140 (C–N stretching), 1120 (C–C stretching), 1050, 1040, 985, 950, 895, 820, 780 (C–H bending; phenyl). U.V/VIS (nm. 190.00 to 500.00): 193, 297, 333.

Moxifloxacin-Cobalt HNMR, FTIR and U.V/VIS:

1H NMR (D₂O) ppm: δ 8.51 (s, 1H; H—2, -CH), 6.98 (s, 1H, H—5, -CH), 4.74 (s, 2H, H–15, -CH2), δ 3.94 (d, 3H, H-10 & 10', CH-CH2, J= 23.7), δ 3.75 (s, 2H, H–13, N–CH2), δ 3.58 (d, H, H-14', N–CH, J= 10.8), 3.42 (s, 3H, – OCH3) δ 3.31 (s, 1H, H-12, -CH2), 2.72 (d, 1H, --NH–, J= 20.4) 1.80 (s, 4H, cyclopropane, -CH2–CH2--), 1.14 (s, 2H, H-11, CH2), 0.76 (s, 1H, cyclopropane, --CH--).

IR (KBr, cm-1): 3320 (O–H stretching of HOH; COOH), 3020 (aromatic C–H stretching), 2930, 2850 (aliphatic C–H stretchings), 1700 (C=O stretching; COOH), 1610 (N–H bending), 1530 (aromatic C–C stretching), 1460 (C=C stretching), 1310, 1350 (aliphatic C–H bending), 1235, 1205 (C–F stretching), 1180 (C–O stretching), 1156 (C–N stretching), 1111 (C–C stretching), 1016, 985, 950, 890 (C–H bending; phenyl).

U.V/VIS (nm. 190.00 to 500.00): 193, 298, 336.

Moxifloxacin-Nickel HNMR, FTIR and U.V/VIS:

1H NMR (D₂O) ppm: δ 8.58 (s, 1H; H—2, -CH), 7.28 (d, 1H, H—5, -CH, J= 13.8), 4.17 (m, 2H, H–15, N–CH2), δ 3.68 (s, 1H, H–14',-CH) 3.57 (t, 2H, H-13, –CH2), δ 3.30 (s, 3H, –OCH3), δ 3.10 (t, 2H,H–10,N–CH2), δ 2.77 (t, 1H, H–10',N–CH–), δ 2.56 (s, 1H, --NH–,), 1.67 (q, 4H, H-11 & H-12, –CH2–CH2--), 0.90 (d, 4H, cyclopropane, CH2–CH2, J= 47.1), 0.76 (s, cyclopropane, –CH).

IR (KBr, cm-1): 3300 (O–H stretching of HOH; COOH), 3005 (aromatic C–H stretching), 2940, 2860 (aliphatic C–H stretchings), 1715 (C=O stretching; COOH), 1620 (N–H bending), 1520 (aromatic C–C stretching), 1460 (C=C stretching), 1310, 1350 (aliphatic C–H bending), 1280 (C–F stretching), 1185 (C–O stretching), 1160 (C–N stretching), 1100 (C–C stretching), 1030, 1002, 955, 870, 805, 730 (C–H bending; phenyl). U.V/VIS (nm. 190.00 to 500.00): 193, 294, 335.

Antibacterial activity:

Agar well diffusion method was carried out to study the antibacterial activity of moxifloxacin and its metal complexes. Test organisms included *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus faecalis*, *Streptococcus pyogenes*, *Corynebacterium diphtheriae*, *Enterobacter aerogenes*, *Salmonella typhi*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Bacterial suspension was prepared by inoculating freshly grown culture into 5ml sterile saline and turbidity was adjusted visually equivalent to 0.5 McFarland standard. This suspension was

then evenly swabbed onto labeled Mueller Hinton agar plates. The plates were allowed to dry for 5 minutes before punching wells with the help of sterile metallic borer (7 mm diameter). The dilutions of test compounds were introduced in wells and allowed to diffuse at room temperature before incubating at 37° C for 24 hours. Antibacterial activity was determined by measuring the diameter of growth inhibition zones (in mm). Growth inhibition was calculated with reference to the positive control i.e. moxifloxacin.

Antioxidant investigation

Freshly prepared 2ml of 0.1mM DPPH radical solution in methanol was added to 2ml solution of synthesized compounds [Moxifloxacin-Zn(I), Ni(VI) and Co(VIII)] of different concentrations (50, 100 and 200 μ g/ml) in methanol. The mixture was shaken vigorously and allowed to stand at room temperature in dark for 30 minutes. DPPH blank and standard compound ascorbic acid were also kept under same condition. The absorbance was recorded in triplicate at 517 nm by using UV/visible spectrophotometer. The DPPH scavenging effect in percentage was calculated by using absorbance value of test, standard and blank in the following equation;

DPPH scavenging effect (%) = Ao - A1/Ao \times 100

Where: A_0 = absorbance of blank, A1= absorbance of test

Results and Discussion: -

Electronic spectra and magnetic measurements

The spectral data (UV-Visible absorption) of the moxifloxacin and moxifloxacin–Zn(I), Ni(VI) and Co(VIII) metal complexes are shown in Methods. The electronic transition of the Moxifloxacin occurred at 292 nm. But on complexation with the different metal ions like Zn(I), Ni(VI) and Co(VIII), new bands appeared between 291 and 299 nm, corresponding to the transitional charge transfer from the Moxifloxacin to the different metal ions. Bands occurred in the region of 297, 294, and 298 nm are assigned to charge transfer transition (L \rightarrow M) for [Zn(MOX₎₂], [Ni(MOX₎₂] and [Co(MOX₎₂] metal complexes respectively (Kondaiah *et al.*, 2017) (Kadyrov *et al.*, 1996; Neda *et al.*, 1996; Sonnenburg *et al.*, 1994).

FTIR spectroscopic studies

The FTIR spectra of metal complexes with Zn(I), Ni(VI) and Co(VIII), (Kunze *et al.*, 2002; C. V. Maftei *et al.*, 2013; I Neda *et al.*, 1993) have displayed major differences compared to FTIR spectra of moxifloxacin. The carboxyl stretches band appears at 3530 cm⁻¹ in the spectrum of moxifloxacin. In the FTIR spectra of Zn(I), Ni(VI) and Co(VIII) and metal complexes the carboxyl stretches band was not recorded at 3530 cm⁻¹ because of the bonding of metal ion with oxygen of carboxylate. One new band appeared for these complexes (Imran *et al.*, 2007; Tulkens *et al.*, 2012), at 200-300 cm⁻¹ below then original, one extra is also seen at between 1600-1620 cm-1 for all complexes.

1H NMR spectroscopic studies

The D₂O solvent is used for recording 1H NMR spectra of moxifloxacin and its metal complexes. In moxifloxacin 1H NMR spectra, the aromatic protons that are H-2 and H-5 are very close to the coordination site of the moxifloxacin. H-2 proton of moxifloxacin appeared, singlet at δ 8.57 ppm and H-5 proton of moxifloxacin noticed at (δ 6.89 ppm) and appeared as a singlet. A multiplet at (δ 4.06 ppm) due to [2H,N–4'–CH2]. The H-14' protons were observed as doublet signal at (δ 3,91 ppm), i.e., [1H,–CH)], H-10 and H-10' protons were observed as multiplet signal at (δ 3.70 ppm), i.e., [3H,(N–CH2–CH--)], a singlet of 3H of OCH 3 group appeared at δ 3.50 ppm. The spectral band of [1H, NH] was shown at δ 2.76 ppm, a triplet at [4H (δ 1.88 ppm)] due to [4H (2H-11, 2H-12 ')] (δ 1.22 ppm)] due to [H, (cyclopropane –CH--)], a multiplet at [2H (δ 1.09 ppm)] due to [2H (Cyclopropane –CH2')] and a quadruplet at [2H (δ 0.91 ppm)] due to [2H (Cyclopropane –CH2')]. Upon addition of a metal, these protons undergo the most significant changes. In the metal complexes, the H-2 proton gives a new signals at δ =8.78, 8.58 and 8.51 ppm while H-5 proton signals were appeared at δ 7.48, 7.28 and 6.98 ppm, respectively, for Zn(I), Ni(VI), and Co(VIII), complexes (Ali *et al.*, 2013; Chiririwa & Muzenda, 2014; Efthimiadou *et al.*, 2006). The above H-2 and H-5 shift is because of the complex formation and also due to difference in the configuration of complexes than moxifloxacin. The physicochemical properties of the metal complexes are shown in Table 1.

Table	1Melting	Points	of All	Metals and	1 Their	Drug	Compl	exes in	Celsius
Lanc	1 Miching	1 Onus	or m	metals and	a inch.	Drug	Compr	CAUS III	Censius

U	U	1	
	Zn	Ni	Со
Metal	290	1455	735
Drug Complex	270	298	248

Antibacterial activity

Antibiotic resistance is one of the major problems in treating bacterial infections. The treatment of such resistant bacterial infections relies on the development of new compounds which are effective against a wide range of grampositive and gram-negative bacteria. In this study, therefore, various metal-moxicillin complexes were prepared and tested for antimicrobial activity.

The moxifloxacin alone showed moderate antibacterial activity for both gram-negative and gram-positive bacteria (Table 2) compared to metal-moxifloxacin complexes which showed higher antibacterial activity (Table 3; Table 4; Table 5). As compared to the parent drug, moxifloxacin, the antibacterial activity of all tested metal complexes increased considerably. Among metal-moxifloxacin complexes, Ni(VI),) and Co(VIII) metal complexes showed higher antibacterial activity compared to Zn(I) metal complexes Table 6.

The Moxi-Zinc complex (Table 3) showed highest activity against C. diphtheriae at the lowest concentration of complex used (MIC; 0.19 ppm). An antibacterial effect was also observed against S. typhi. (MIC; 0.38) compared to parent compound which showed no activity against it.

The Moxi-Ni complex showed highest antibacterial effect against S. aureus and S. epidermidis, (MIC; 0.19 ppm). Similarly, a higher antibacterial effect was also obtained against S. typhi (MIC; 1.55 ppm) Table 4.

The Moxi-Co complex were found to be most effective against E. aerogenes and C. diphtheriae (MIC; 0.19 ppm). Others including S. faecalis and K. pneumonia also showed higher sensitivity to this compound (MIC; 0.77 ppm) Table 5.

This study showed an overall high effectivity of metal-moxifloxicin componds against gram-negative and grampositive bacteria and could play a key role in new drug development. One of the major development in recent study is the effects of metal-moxi complexes against the *Salmonella enterica* serovar typhi, which are remarkably high (ranked as Moxi-Ni > Moxi-Co > Moxi-Zn). Emergence of drug resistant strains of S. typhi, classified as extensively drug resistance (XDR) typhoid, resistant against chloramphenicol, ampicillin, and trimethoprimsulfamethoxazole along with third-generation cephalosporins and fluoroquinolones are at rise (Klemm *et al.*, 2018) with multiple cases reported in various parts of Pakistan (Ahmed, 2018). In this connection the discovery of highly effective metal-moxi complexes, against not only XDR S. typhi but also against other multidrug resistant organisms, is quite promising. While existing drug therapies are exhausting, these compounds could prove to be novel effective treatment options.

Moxifloxacin						
Dilution (ppm)	0.19	0.38	0.77	1.55	3.125	6.25
Organism	Zone of inhibition (mm)					
S. aureus	-	-	10	13	20	23
S. epidermidis	-	-	-	13	16	20
S. faecalis	-	-	10	12	14	16
S. pyogenes	-	-	12	16	18	20
C. diphtheriae	-	-	-	-	-	-
P. aeuroginosa	-	-	-	-	-	-
E. aerogenes	-	-	-	-	12	16
K. pneumonia	-	-	-	-	16	19
S. typhi	-	-	-	-	-	-

 Table 2: -Antibacterial effect of Moxifloxacin

Table 5. -Antibacterial effect of Moxi-Zine complex	Table 3:	-Antibacterial	effect of	Moxi-zinc	complex
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Moxi-Zinc Complex						
Dilution (ppm)	0.19	0.38	0.77	1.55	3.125	6.25
Organism			Zone of inl	nibition (mm	ı)	
S. aureus	14	16	20	24	26	30
S. epidermidis	18	20	22	24	28	Clear
S. faecalis	-	12	16	20	22	25

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S. pyogenes	11	14	22	26	28	30
C. diphtheriae	20	24	30	32	Clear	Clear
P. aeuroginosa	-	-	-	12	14	20
E. aerogenes	16	18	20	22	24	26
K. pneumonia	12	16	20	24	26	28
S. typhi	-	12	16	20	22	24

Table 4: -Antibacterial effect of Moxi-Nickel complex

Moxi-Nickel Complex						
Dilution (ppm)	0.19	0.38	0.77	1.55	3.125	6.25
Organism			Zone of inl	nibition (mm	l)	
S. aureus	22	24	26	28	30	34
S. epidermidis	22	24	28	30	32	34
S. faecalis	12	16	18	20	22	24
S. pyogenes	12	14	18	20	22	24
C. diphtheriae	12	14	18	22	26	28
P. aeuroginosa	-	-	14	18	20	24
E. aerogenes	12	14	16	20	26	28
K. pneumonia	16	18	20	22	24	30
S. typhi	16	18	20	22	24	26

Table 5: -Antibacterial effect of Moxi-Cobalt complex

Moxi-Cobalt Complex						
Dilution (ppm)	0.19	0.38	0.77	1.55	3.125	6.25
Organism			Zone of inl	nibition (mm	l)	
S. aureus	14	16	18	22	24	26
S. epidermidis	12	14	18	24	28	30
S. faecalis	18	20	22	26	28	30
S. pyogenes	22	28	32	34	-	-
C. diphtheriae	28	30	34	38	-	-
P. aeuroginosa	-	10	14	20	24	29
E. aerogenes	22	26	28	30	32	34
K. pneumonia	18	20	22	24	26	28
S. typhi	12	14	20	22	24	30

Table 6: -The antibacterial strength of metal-moxifloxacin complexes.

Organism	Metal Moxifloxacin Complex strength
S. aureus	Ni(VI) > Zn(I), >Co(VIII),
S. epidermidis	Ni(VI) > Zn(I) > Co).
S. faecalis	Co(VIII) > Ni(VI) > Zn(I)
S. pyogenes	Co(VIII) > Ni(VI) > Zn(I)
C. diphtheriae	Co(VIII), > Zn(I) > Ni(VI)
P. aeuroginosa	Co(VIII > Ni(VI) > Zn(I).
E. aerogenes	Co(VIII) > Zn(I) > Ni(VI),
K. pneumonia	Co(VIII), Ni(VI) > Zn(I),
S. typhi	Ni(VI) > Co(VIII) > Zn(I),

Antioxidant investigation:

Synthesis of new compounds having potential to protect the body from oxidative damage by neutralizing the free radicals, have become an important task in inorganic synthesis. Natural and synthetic antioxidants reduced the risk of chronic diseases by inhibiting the oxidation of substrate (Odeyemi *et al.*, 2017). Various in vitro procedures provide a useful indication of antioxidant capabilities of compound by analyzing the capacity of compounds for radical capture or inhibition of radical formation. The in-vitro DPPH method is preferred over other methods because this method is convenient, reliable and fast. The DPPH free radical is scavenged by receiving hydrogen or

electron from antioxidant and become colorless in reduced form (Mishra *et al.*, 2012). The percent inhibitions with relation to concentration of synthesized compounds along standard ascorbic acid have been reported in figure. Our analytical data showed (Table 7) that with increase in concentration percent inhibition also increases, the maximum inhibition was found between 15-20 μ g/ml (Biswas *et al.*, 2010). Antioxidant activity influenced by the substitution at carbonyl group with metal groups, presence of different metal ions potentiates the scavenging effect. Synthesized compounds showed moderate to good antioxidant activates as compared with standard ascorbic acid (Table 7).

S. No.	Code	$IC_{50}+SEM^{a}(\mu g/ml)$
1	Standard	1.65 ± 0.16
2	Zn	14.88 ± 0.31
3	Ni	17.06 ± 0.19
4	Со	11.18 ± 0.32

Table 7: -Antioxidant activities of moxi- metal complexes

Conclusions: -

In the above research work, Zn(I), Ni(VI) and Co(VIII) moxifloxacin metal complexes were prepared and characterized by 1H-NMR, FTIR and UV-Vis. The IR spectra lead to the conclusion that in all complexes, ligand acts as a bidentate. These metal complexes have shown significant antibacterial effects against the tested bacteria. The moxifloxacin–Ni(VI), and Co(VIII) metal complexes showed high antibacterial activity compared to moxifloxacin-Zn(I) and moxifloxacin). The antibacterial activity indicates the metal complexes have more biological activity than parent drug (moxifloxacin). Antioxidant activity influenced by the substitution at carbonyl group with metal groups, presence of different metal ions potentiates the scavenging effect. Synthesized compounds showed moderate to good antioxidant activates as compared with standard ascorbic acid. Thus moxifloxacin metal compounds have potential to be novel antibacterial agents.

References:-

- 1. Ahmad M. (2018). Pakistan is racing to combat the world's first extensively drug-resistant typhoid outbreak. Sci Am. March 14, 2018
- 2. Ali, H. R. H., Ali, R., Batakoushy, H. A., & Derayea, S. M. (2017). Spectroscopic Analysis and Antibacterial Evaluation of Certain Third Generation Cephalosporins Through Metal Complexation. Analytical Chemistry Letters, 7(4), 445-457.
- Ali, K. A., Abd-Elzaher, M. M., & Mahmoud, K. (2013). Synthesis and anticancer properties of silver (I) complexes containing 2, 6-Bis (substituted) pyridine derivatives. International journal of medicinal chemistry, 2013.
- 4. Andriole, V. T. (2005). The Quinolones: Past, Present, and Future. Clinical Infectious Diseases, 41(Supplement_2), S113-S119. doi: 10.1086/428051
- 5. Biswas, M., Haldar, P. K., & Ghosh, A. K. (2010). Antioxidant and free-radical-scavenging effects of fruits of Dregea volubilis. Journal of natural science, biology, and medicine, 1(1), 29.
- 6. Blair, J. M., Webber, M. A., Baylay, A. J., Ogbolu, D. O., & Piddock, L. J. (2015). Molecular mechanisms of antibiotic resistance. Nature reviews microbiology, 13(1), 42.
- 7. Chiririwa, H., & Muzenda, E. (2014). Synthesis, Characterization of Gold (III) Complexes and an in vitro Evaluation of their Cytotoxic Properties.
- 8. Cuprys, A., Pulicharla, R., Brar, S. K., Drogui, P., Verma, M., & Surampalli, R. Y. (2018). Fluoroquinolones metal complexation and its environmental impacts. Coordination Chemistry Reviews, 376, 46-61.
- 9. Demir, S., Gelincik, A., Akdeniz, N., Aktas-Cetin, E., Olgac, M., Unal, D., . . . Deniz, G. (2017). Usefulness of in vivo and in vitro diagnostic tests in the diagnosis of hypersensitivity reactions to quinolones and in the evaluation of cross-reactivity: a comprehensive study including the latest quinolone gemifloxacin. Allergy, asthma & immunology research, 9(4), 347-359.
- 10. Efthimiadou, E. K., Karaliota, A., & Psomas, G. (2008). Mononuclear dioxomolybdenum (VI) complexes with the quinolones enrofloxacin and sparfloxacin: Synthesis, structure, antibacterial activity and interaction with DNA. Polyhedron, 27(1), 349-356.
- Efthimiadou, E. K., Sanakis, Y., Raptopoulou, C. P., Karaliota, A., Katsaros, N., & Psomas, G. (2006). Crystal structure, spectroscopic, and biological study of the copper (II) complex with third-generation quinolone antibiotic sparfloxacin. Bioorganic & medicinal chemistry letters, 16(14), 3864-3867.

- 12. Elshafie, H. S., Sakr, S. H., Sadeek, S. A., & Camele, I. (2019). Biological investigations and spectroscopic studies of new Moxifloxacin/Glycine-Metal complexes. Chemistry & biodiversity.
- 13. Fernandes, P., & Martens, E. (2017). Antibiotics in late clinical development. Biochemical pharmacology, 133, 152-163.
- 14. Imran, M., Iqbal, J., Iqbal, S., & Ijaz, N. (2007). In vitro antibacterial studies of ciprofloxacin-imines and their complexes with Cu (II), Ni (II), Co (II), and Zn (II). Turkish journal of biology, 31(2), 67-72.
- Kadyrov, A., Neda, I., Kaukorat, T., Sonnenberg, R., Fischer, A., Jones, P., & Schmutzler, R. (1996). New Phospholene and Phosphepine Derivatives from lambda[^] 3-Phosphorus Compounds and Hexafluoroacetone or Perfluorinated -Diketones. Chemische Berichte, 129, 725-732.
- 16. Kelly, F. (1998). Use of antioxidants in the prevention and treatment of disease. Journal of the International Federation of Clinical Chemistry, 10(1), 21-23.
- 17. Klemm, E. J., Shakoor, S., Page, A. J., Qamar, F. N., Judge, K., Saeed, D. K., ... Baker, S. (2018). Emergence of an extensively drug-resistant Salmonella enterica serovar Typhi clone harboring a promiscuous plasmid encoding resistance to fluoroquinolones and third-generation cephalosporins. MBio, 9(1), e00105-00118.
- 18. Kondaiah, S., Bhagavanth Reddy, G., Rajesh, D., & Vijayakumr, B. (2017). Synthesis, characterization and biological activity of moxifloxacin-cu (II) metal complex. IJETSR, 4(12), 1138-1145.
- Kunze, C., Neda, I., Freytag, M., Jones, P. G., & Schmutzler, R. (2002). Mono-and Binuclear Rhodium and Platinum Complexes of 1, 3, 5-Trimethyl-1, 3, 5-triaza-2σ3λ3-phosphorin-4, 6-dionyloxy-substituted Calix [4] arenes. Zeitschrift für anorganische und allgemeine Chemie, 628(3), 545-552.
- Luepke, K. H., Suda, K. J., Boucher, H., Russo, R. L., Bonney, M. W., Hunt, T. D., & Mohr III, J. F. (2017). Past, present, and future of antibacterial economics: increasing bacterial resistance, limited antibiotic pipeline, and societal implications. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 37(1), 71-84.
- Maftei, C. V., Fodor, E., Jones, P. G., Franz, M. H., Kelter, G., Fiebig, H., & Neda, I. (2013). Synthesis and characterization of novel bioactive 1, 2, 4-oxadiazole natural product analogs bearing the N-phenylmaleimide and N-phenylsuccinimide moieties. Beilstein journal of organic chemistry, 9, 2202.
- Maftei, E., Maftei, C. V., Jones, P. G., Freytag, M., Franz, M. H., Kelter, G., . . . Neda, I. (2016). Trifluoromethylpyridine-Substituted N-Heterocyclic Carbenes Related to Natural Products: Synthesis, Structure, and Potential Antitumor Activity of some Corresponding Gold (I), Rhodium (I), and Iridium (I) Complexes. Helvetica Chimica Acta, 99(6), 469-481.
- 23. Mihorianu, M., Franz, M. H., Jones, P. G., Freytag, M., Kelter, G., Fiebig, H. H., . . . Neda, I. (2016). N-Heterocyclic carbenes derived from imidazo-[1, 5-a] pyridines related to natural products: synthesis, structure and potential biological activity of some corresponding gold (I) and silver (I) complexes. Applied Organometallic Chemistry, 30(7), 581-589.
- 24. Mishra, K., Ojha, H., & Chaudhury, N. K. (2012). Estimation of antiradical properties of antioxidants using DPPH assay: A critical review and results. Food chemistry, 130(4), 1036-1043.
- Murray, G. L., Bradshaw, C. S., Bissessor, M., Danielewski, J., Garland, S. M., Jensen, J. S., . . . Tabrizi, S. N. (2017). Increasing macrolide and fluoroquinolone resistance in Mycoplasma genitalium. Emerging infectious diseases, 23(5), 809.
- 26. Nakamoto, K., & McCarthy, P. J. (1968). Spectroscopy and structure of metal chelate compounds: Wiley.
- Neda, I., Melnicky, C., Vollbrecht, A., & Schmutzler, R. (1996). An unusual N-alkylation reaction during the oxidative addition of hexafluoroacetone and tetrachloro-o-benzoquinone to P-bis (2-chloroethyl) aminosubstituted λ3P-compounds. Synthesis, 1996(04), 473-474.
- 28. Neda, I., Plinta, H. J., & Schmutzler, R. (1993). Reactions of 1, 3-Dialkyl-1, 3-diaza-2-chloro-5, 6-benzo-1, 3, 2-phosphorinan-4-ones; Preparation of P (III) Derivatives. ChemInform, 24(29), no-no.
- 29. Odeyemi, S., Afolayan, A., & Bradley, G. (2017). Phytochemical analysis and anti-oxidant activities of Albuca bracteata Jacq. and Albuca setosa Jacq bulb extracts used for the management of diabetes in the Eastern Cape, South Africa. Asian Pacific Journal of Tropical Biomedicine, 7(6), 577-584.
- 30. Rafique, S., Idrees, M., Nasim, A., Akbar, H., & Athar, A. (2010). Transition metal complexes as potential therapeutic agents. Biotechnology and Molecular Biology Reviews, 5(2), 38-45.
- Refaat, H. M., El-Badway, H. A., & Morgan, S. M. (2016). Molecular docking, geometrical structure, potentiometric and thermodynamic studies of moxifloxacin and its metal complexes. Journal of Molecular Liquids, 220, 802-812.
- Sadeek, S. A., El-Shwiniy, W. H., & El-Attar, M. S. (2011). Synthesis, characterization and antimicrobial investigation of some moxifloxacin metal complexes. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 84(1), 99-110.

- 33. Skuredina, A., Le-Deygen, I., Uporov, I., & Kudryashova, E. (2017). A study of the physicochemical properties and structure of moxifloxacin complex with methyl-β-cyclodextrin. Colloid Journal, 79(5), 668-676.
- 34. Soayed, A. A., Refaat, H. M., & El-Din, D. A. N. (2013). Metal complexes of moxifloxacin-imidazole mixed ligands: Characterization and biological studies. Inorganica Chimica Acta, 406, 230-240.
- 35. Sonnenburg, R., Neda, I., Fischer, A., Jones, P., & Schmutzler, R. (1994). Compounds Involving the 5, 6-Benzo-1, 3, 2-diazaphosphorinane-4-one Ring System: Synthesis of 2-Chloro-, 2-N, N-Dimethylamino-and 2-Bis-(2-chloroethyl) amino-Substituted Derivatives with Three-and Four-Coordinated Phosphorus. ChemInform, 25(48), no-no.
- 36. Tiwari, A. K. (2001). Imbalance in antioxidant defence and human diseases: Multiple approach of natural antioxidants therapy. Current science, 1179-1187.
- 37. Tulkens, P. M., Arvis, P., & Kruesmann, F. (2012). Moxifloxacin safety. Drugs in R&D, 12(2), 71-100.
- 38. Ventola, C. L. (2015). The antibiotic resistance crisis: part 1: causes and threats. Pharmacy and Therapeutics, 40(4), 277.