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RESEARCH ARTICLE

SYNTHESIS, CHARACTERIZATION AND ASSESSMENT OF BIOLOGICAL ACTIVITIES OF INORGANIC DERIVATIVES OF DIHYDROQUINOLINE 3 CARBOXYLIC ACID

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ABSTRACT

To develop new drugs that inhibit growth of pathogenic microorganisms, metal derivatives of Dihydroquinoline 3 carboxylic acid are assessed. Metal complexes with the fourth-generation fluoroquinolone antibacterial agent moxifloxacin (MOXI) or 7-[(4aS,7aS)-1,2,3,4,4a,5,7,7a-octahydro-1H-pyrido[3,4-b]pyridin-6-yl]-1-cyclopropyl-6-fluoro-8-methoxy-4-oxoquinoline-3-carboxylic acid have been synthesized and characterized with physicochemical and spectroscopic techniques such as TLC, FTIR, ¹H-NMR, UV-Vis spectroscopy and Mass spectroscopy and assessed for antioxidant and antibacterial effects. Both ¹H NMR and FTIR spectra clearly showed that Moxi-metal complexes are formed due to change in their carboxyl stretching band in IR, H-2 and H-5 peak position in ¹H NMR. All the Moxi-metal complexes showed significant antibacterial and antioxidant effects. Among all metal complexes tested Moxi-Mo showed remarkable antibacterial effect and Moxi-Cd complexes showed good antibacterial activity. The Moxi-Cd complex showed antioxidant effects almost similar to that of standard agent (IC₅₀ = 8.26 µg/ml), Moxi-Mo (IC₅₀ = 3.01 µg/ml) and Moxi-Mg (IC₅₀ = 3.62 µg/ml) metal complexes showed higher antioxidant activity than the parent drug.

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INTRODUCTION

Resistant bacteria effect the world's health system severally. The antibiotics which were used previously for saving lives of numerous patients around the world have lost their effectiveness due to the development of resistant bacterial strains. The main reasons are the overuse and misuse of available antibiotics. Besides the decrease in development of new antibiotics is another major issue (Blair, Webber, Baylay, Ogbolu, & Piddock, 2015; Ventola, 2015). In last few decades, some antibiotics such as tigecycline and tedizolid have been synthesized and FDA approved them but they are only effective against Gram-positive bacteria (Luepke et al., 2017). Moxifloxacin, gemifloxacin and gatifloxacin (broad spectrum Dihydroquinoline) were marketed in 2004 (Andriole, 2005; Kondaiah, Bhagavanth Reddy, Rajesh, & Vijayakumr, 2017). Several microorganisms in past years have shown resistance against moxifloxacin (Luepke et al., 2017; Murray et al., 2017). To deal with drug resistance, new drugs need to be developed with new drug delivery system. Development of new drug takes a long time, at least a decade, and millions of dollars which makes it unfeasible (Fernandes & Martens, 2017).

It is, therefore, easy to modify the existing antibiotics with better drug delivery system rather than to develop a new one to overcome the problem of drug resistance and also enhance the drug effectiveness (Kondaiah et al., 2017; Skuredina, Le-Deygen, Uporov, & Kudryashova, 2017a). Different drugs were modified by conjugating with both inorganic and organic substances physically or chemically (Cuprys et al., 2018; Refaat, El-Badway, & Morgan, 2016; Skuredina, Le-Deygen, Uporov, & Kudryashova, 2017b). Former method i.e. the inorganic complexation overcomes the problem of time consumption, ease to carry out as well as less expenditure as compared to organic complexation (H. R. H. Ali, Ali, Batakoushy, & Derayea, 2017; Elshafie, Sakr, Sadeek, & Camele, 2019). Metal complexes of Moxifloxacin have drawn attention of many researchers therefore setting grounds for development of new drugs. Sadeek et al., (2011) reported activity of moxifloxacin-metal complexes including yttrium, palladium, titanium and cerium against various microbes. Soayed et al., (2013) synthesized and characterized moxifloxacin-imidazole-metal complexes and also reported their biological activities. In this study metal complexation of moxifloxacin is done to develop new compounds and assess their biological activities to address problem of drug resistance.

MATERIALS AND METHODS

Standard drug (moxifloxacin) and all metals (Cd, Cu, Mg and Mo) were purchased from Sigma-Aldrich Limited.

Synthesis: The ratio of drug and metal was 2:1 by dissolving them in solvent (methanol) individually. Both drug and metal solutions were refluxed in a single round bottom flask (8 -12 hrs) by maintaining temperature in between 55-60°C and stirring throughout whole reaction. The final product was evaporated to remove extra solvent and precipitated using chilled chloroform and at the end the final product was recrystallized.

Spectral Characterization

HNMR, FTIR and U.V/VIS of Moxi-metal complexes were as shown in Table 1, Table 2 and Table 3.

Antibacterial effects: Antibacterial assay of the test compounds was performed by agar diffusion method (Smania *et al.*, 1995). Briefly, bacterial cultures were grown in Mueller-Hinton agar plates and culture suspension was prepared by transferring few colonies in 5ml sterile saline and adjusting the turbidity equal to McFarland 0.5 index. Agar plates (Mueller-Hinton) were swabbed with above prepared suspension. With the help of 7mm diameter borer wells were punched in the agar plates. The parent drug and their metal complexes were added in agar plate wells before incubating at 37°C for 24 hrs. Next day results were noted in terms of diameter of inhibition zone.

Antioxidant investigation: DPPH solution (2ml of 0.1mM) was mixed with both parent drug methanolic solution and metal derivatives of Moxifloxacin (200ppm, 100 ppm and 50 ppm). The mixtures were mixed vigorously and left for half an hour at room temperature. Similarly, blank and ascorbic acid (standard compound) were processed in the same manner. The absorbance band at 517 nm was recorded by using UV/Vis spectrophotometer. All sample, blank and standard's absorbance was employed to compute the DPPH scavenging effects (percentage) with help of DPPH scavenging effect (%) formula;

$$\text{DPPH scavenging effect (\%)} = (A_0 - A_1)/A_0 \times 100$$

A_0 = absorbance of DPPH,

A_1 = absorbance of Parent drug and their metal derivatives

Statistical Study: All data of study for continuous variables were written in mean \pm S.D, the variation among the activities was evaluated using IC_{50} . The MS Excel were used for the complete analysis.

RESULTS

UV/Visible Spectroscopic studies: At 292nm an electronic change is seen for moxifloxacin in UV/Vis spectroscopy but in case of metal complexation the electronic transition was seen between 294 and 298nm due to the complexation of drug with metal (Kondaiah *et al.*, 2017). The electronic transition at 296 for both $[Cd (MOX)_2][Mg (MOX)_2]$, 294 for $[Cu (MOX)_2]$, and 298 nm for $[Mo (MOX)_2]$ was observed (Kondaiah *et al.*, 2017).

FTIR spectroscopic studies: The carbonyl group of drug was used to bind with metal ions, so at 3530cm^{-1} carboxyl stretching was seen for drug but the complex of drug-metal observed the carboxyl band at $200\text{--}300\text{ cm}^{-1}$ below or above then 3530 cm^{-1} due to carboxylate's oxygen bonds with metal ion (Kunze, Neda, Freytag, Jones, & Schmutzler, 2002; Maftei *et al.*, 2013).

The complexation is confirmed (Figure 1) appearing a band at $1600\text{--}1640\text{ cm}^{-1}$ (Imran, Iqbal, Iqbal, & Ijaz, 2007; Tulkens, Arvis, & Kruesmann, 2012).

^1H NMR spectroscopic studies: The two aromatic protons (H-2 and H-5) of moxifloxacin were changed after complexation. H-2 proton signal in metal complexes shifts at $\delta = 8.7\mu\text{g/ml}$, $8.31\mu\text{g/ml}$, $8.47\mu\text{g/ml}$ and $8.52\mu\text{g/ml}$ on other hand the H-5 proton signal shifted at $\delta = 7.15\mu\text{g/ml}$, $6.88\mu\text{g/ml}$, $7.61\mu\text{g/ml}$ and $7.63\mu\text{g/ml}$, respectively, for Cd, Cu, Mg and Mo complexes (K. A. Ali, Abd-Elzaher, & Mahmoud, 2013; Chiririwa & Muzenda, 2014; Efthimiadou *et al.*, 2006).

Antibacterial activity: Bacteria acquire resistance to antibiotics which is attributed by irrational and indiscriminate use of antibiotics. This causes problem in treating such infections with available drugs. This calls for the development of newer broad spectrum compounds to deal with a wide range of bacteria. In this research we synthesized metal complexes of Moxifloxacin and tested their antimicrobial effects against various bacteria. Antibacterial assay of parent compound Moxifloxacin showed resistance of pathogens including *S. typhi*, *C. diphtheriae* and opportunistic bacteria *P. aeruginosa*. However, moxifloxacin exhibited a modest effect against other bacteria (Gram-positive and Gram-negative) (Table. 4). All the metal complexes of moxifloxacin showed much higher antibacterial activity compared to parent compound Moxifloxacin (Table. 5; Table. 6; Table. 7; and Table. 8). The Moxi-Cd complex (Table. 5) exhibited highest activity against *S. epidermidis* (MIC $0.19\mu\text{g/ml}$) followed by *S. aureus* and *S. pyogenes*. This compound showed antibacterial effect against *S. typhi* (MIC $1.55\mu\text{g/ml}$) compared to parent compound which was totally ineffective. The Moxi-Cu (Table. 6) showed a very pronounced effect against *C. diphtheriae* (MIC $0.19\mu\text{g/ml}$). Significant antibacterial effects were obtained against all the organisms tested including *S. typhi* (MIC $0.38\mu\text{g/ml}$) compared to parent compound. The Moxi-Mg complex shown in Table. 7 had greatest antibacterial effects against *S. aureus* and *K. pneumonia* followed by *E. aerogenes* (MIC $0.19\mu\text{g/ml}$) and *S. typhi* ($0.77\mu\text{g/ml}$). The Moxi-Mo showed the highest activity at lowest concentration used against all the organisms tested (Table. 8 and Table. 9). It exhibited pronounced antibacterial activity among all the compounds tested as well as compared to parent compound Moxifloxacin. The data generated in this study shows the high antibacterial activity of the metal conjugated Moxifloxacin compounds. As it is evident that most compounds showed an enhanced antibacterial effect against all gram-positive and gram-negative organisms compared to parent compound Moxifloxacin. Secondly, these compounds were found to be effective against *S. typhi* which parent compound was unable to inhibit and among the compounds tested the effectivity pattern was Moxi-Mo > Moxi-Cu > Moxi-Mg > Moxi-Cd. Moxi-metal compounds synthesized in this study are quite promising. The effectivity of these compounds renders them for new options of drug development, not only for *S. typhi*, but also against various other pathogens and promising to be new treatment alternatives.

Antioxidant investigation: The need of time is to develop new drug derivatives having good antioxidant effects to neutralize the free radicals to protect body from oxidative damages. Antioxidants (Both synthetic and natural) block oxidation of substrates thus lowering the chances of chronic disease development (Odeyemi, Afolayan, & Bradley, 2017). Various methods are employed to examine the ability of metal derivatives to scavenge radicals and identify the antioxidant capabilities of compounds to inhibit their formation, DPPH cleaning method is found to be the most preferred method out of other methods, due to ease to perform, well grounded and quick. The reduced form of DPPH is colorless before getting electron or hydrogen from antioxidant (Mishra, Ojha, & Chaudhury, 2012). The results shown in Table 10 indicated increase in percent inhibition with the increase in concentration i.e. directly proportional to each other whereas the limit of maximum inhibition was $15\text{--}20\mu\text{g/ml}$ (Biswas, Halder, & Ghosh, 2010). The Moxi-Cd complex showed antioxidant effects almost similar to that of standard agent ($IC_{50} = 8.26\mu\text{g/ml}$), Moxi-Mo ($IC_{50} = 3.01\mu\text{g/ml}$), Moxi-Mg ($IC_{50} = 3.62\mu\text{g/ml}$) and Moxi-Cu ($IC_{50} = 19.73\mu\text{g/ml}$) metal complexes showed higher antioxidant activity than the parent drug.

Table 1. ^1H NMR (D_2O) $\mu\text{g/ml}$

Complexes	Moxifloxacin	Moxi-Cd	Moxi-Cu	Moxi-Mg	Moxi-Mo
H-2	δ 8.57 s	δ 8.70 s	δ 8.31 s	δ 8.47 s	δ 8.52 s
H-5	δ 6.89 d (J=13.8)	δ 7.15 s	δ 6.88 s	δ 7.61 s	δ 7.63 q
H-15	δ 4.67 s	δ 4.70 s	δ 4.64 s	δ 4.50 s	δ 4.44 s
H-13	δ 4.06 m	δ 3.93 m	δ 3.65 s	δ 4.29 s	δ 4.31 s
H-14'	δ 3.91 d (J=4.2)	δ 3.93 m	δ 3.48 d (J= 10.8)	δ 3.54 d(J= 10.8)	δ 3.44 d(J= 6.1)
H-10 & H-10'	δ 3.70 m	δ 3.31 (H-10', d, J= 28.8) δ 3.26 (H-10, s)	δ 3.84 d (J= 23.7)	δ 3.45 t and δ 2.68 s	δ 3.41 s and δ 2.61 s
OCH_3	δ 3.50 s	δ 3.56 s	δ 3.32 s	δ 3.06 s	δ 3.09 s
NH	δ 2.76 d (J=3.3)	δ 2.80 s	δ 2.62 d (J= 20.4)	2.61 s	δ 3.23 t
H-11 & H12	δ 1.88 t	δ 1.19 s	1.04 s	δ 0.83 s	δ 0.77 s
Cyclo propane	δ 1.22 q, δ 1.09 m and δ 0.91 q.	δ 1.86 s	δ 1.70 s and δ 0.66 s	δ 1.05 q and δ 0.87 s	δ 1.02 q and δ 0.81 s

s: singlet, d: doublet, m: multiplet, q: quartlet, t: triplet

Table 2: FTIR (cm^{-1} , KBr)

Complexes	Moxifloxacin	Moxi-Cd	Moxi-Cu	Moxi-Mg	Moxi-Mo
ST OF O-H (COOH)	3530	3710	3170	3330	3230
ST OF C-H (Aromatic group)	3156	3010	3030	3010	3030
ST OF C-H (Aliphatic group)	2978-2800	2920	2930	2930	2980
ST OF C=O (COOH)	1709	1640	1700	1705	1701
BDOF N-H	1620	1620	1600	1610	1616
ST OF C-C (Aromatic group)	1592-1533	1525	1510	1520	1523
ST OF C=C (Aromatic group)	1490	1465	1440	1470	1473
BD OF C-H (Aliphatic group)	1422-1323	1360	1340	1345	1335
ST OF C-F	1245	1215	1290	1205	1215
ST OF C-O	1184	1165	1190	1180	1165

ST: stretching, BD: bending

Table 3: U.V/Vis Electronic Transitions, Melting Point And Percentage Yield

Complexes	Moxifloxacin	Moxi-Cd	Moxi-Cu	Moxi-Mg	Moxi-Mo
U.V/Vis	292	296	294	296	298
M.Point	238-242 $^{\circ}\text{C}$	266 $^{\circ}\text{C}$	145 $^{\circ}\text{C}$	145 $^{\circ}\text{C}$	238 $^{\circ}\text{C}$
Yield	---	88%	91%	83%	89%

Table 4: Antibacterial Effects of Moxifloxacin

Dilution ($\mu\text{g/ml}$)	0.19	0.38	0.77	1.55	3.125	6.25
Strains						
<i>S. aureus</i>	-	-	10 (\pm 0.10)	13 (\pm 0.13)	20 (\pm 0.14)	23 (\pm 0.15)
<i>S. epidermidis</i>	-	-	-	13 (\pm 0.13)	16 (\pm 0.13)	20 (\pm 0.14)
<i>E. faecalis</i>	-	-	10 (\pm 0.11)	12 (\pm 0.13)	14 (\pm 0.19)	16 (\pm 0.14)
<i>S. pyogenes</i>	-	-	12 (\pm 0.12)	16 (\pm 0.15)	18 (\pm 0.17)	20 (\pm 0.14)
<i>C. diphtheriae</i>	-	-	-	-	-	-
<i>P. aeruginosa</i>	-	-	-	-	-	-
<i>E. aerogenes</i>	-	-	-	-	12 (\pm 0.12)	16 (\pm 0.14)
<i>K. pneumoniae</i>	-	-	-	-	16 (\pm 0.14)	19 (\pm 0.14)
<i>S. typhi</i>	-	-	-	-	-	-

- = no activity

Zone of inhibition = mm \pm SEM

Table 5: Antibacterial Effects of Moxi-Cd complex

Dilution ($\mu\text{g/ml}$)	0.19	0.38	0.77	1.55	3.125	6.25
Strains						
<i>S. aureus</i>	18 (\pm 0.12)	20 (\pm 0.14)	22 (\pm 0.14)	24 (\pm 0.14)	26 (\pm 0.15)	28 (\pm 0.15)
<i>S. epidermidis</i>	20 (\pm 0.14)	22 (\pm 0.14)	26 (\pm 0.16)	28 (\pm 0.16)	30 (\pm 0.16)	32 (\pm 0.16)
<i>E. faecalis</i>	16 (\pm 0.10)	20 (\pm 0.11)	24 (\pm 0.11)	26 (\pm 0.12)	28 (\pm 0.12)	30 (\pm 0.13)
<i>S. pyogenes</i>	18 (\pm 0.11)	20 (\pm 0.11)	24 (\pm 0.16)	28 (\pm 0.12)	40 (\pm 0.23)	Clear
<i>C. diphtheriae</i>	-	-	-	-	-	-
<i>P. aeruginosa</i>	-	-	-	10 (\pm 0.10)	14 (\pm 0.11)	18 (\pm 0.12)
<i>E. aerogenes</i>	14 (\pm 0.10)	16 (\pm 0.11)	18 (\pm 0.12)	20 (\pm 0.12)	22 (\pm 0.13)	24 (\pm 0.13)
<i>K. pneumoniae</i>	10 (\pm 0.10)	16 (\pm 0.12)	18 (\pm 0.13)	20 (\pm 0.14)	22 (\pm 0.12)	24 (\pm 0.12)
<i>S. typhi</i>	-	-	-	12 (\pm 0.11)	14 (\pm 0.11)	18 (\pm 0.12)

- = no activity

Zone of inhibition = mm \pm SEM

Table 6: Antibacterial Effects of Moxi-Cu complex

Dilution ($\mu\text{g/ml}$)	0.19	0.38	0.77	1.55	3.125	6.25
Strains						
<i>S. aureus</i>	10 (\pm 0.10)	16 (\pm 0.11)	18 (\pm 0.11)	20 (\pm 0.14)	22 (\pm 0.14)	24 (\pm 0.14)
<i>S. epidermidis</i>	10 (\pm 0.10)	14 (\pm 0.11)	18 (\pm 0.11)	24 (\pm 0.12)	26 (\pm 0.12)	32 (\pm 0.16)
<i>E. faecalis</i>	14 (\pm 0.11)	16 (\pm 0.12)	18 (\pm 0.13)	20 (\pm 0.14)	26 (\pm 0.15)	28 (\pm 0.15)
<i>S. pyogenes</i>	16 (\pm 0.11)	20 (\pm 0.11)	24 (\pm 0.12)	26 (\pm 0.12)	28 (\pm 0.12)	30 (\pm 0.13)
<i>C. diphtheriae</i>	28 (\pm 0.15)	30 (\pm 0.16)	+	+	+	+
<i>P. aeruginosa</i>	10 (\pm 0.10)	12 (\pm 0.10)	18 (\pm 0.14)	20 (\pm 0.15)	22 (\pm 0.15)	26 (\pm 0.16)
<i>E. aerogenes</i>	12 (\pm 0.10)	14 (\pm 0.11)	20 (\pm 0.14)	22 (\pm 0.14)	24 (\pm 0.14)	26 (\pm 0.14)
<i>K. pneumoniae</i>	-	10 (\pm 0.10)	14 (\pm 0.10)	16 (\pm 0.11)	18 (\pm 0.12)	22 (\pm 0.12)
<i>S. typhi</i>	-	12 (\pm 0.10)	16 (\pm 0.10)	18 (\pm 0.11)	24 (\pm 0.12)	26 (\pm 0.12)

- = no activity

+ = no growth

Zone of inhibition = mm \pm SEM

Table 7: Antibacterial Effects of Moxi-Mg complex

Dilution ($\mu\text{g/ml}$)	0.19	0.38	0.77	1.55	3.125	6.25
Strains						
<i>S. aureus</i>	14 (\pm 0.11)	18 (\pm 0.11)	20 (\pm 0.14)	23 (\pm 0.12)	26 (\pm 0.16)	28 (\pm 0.15)
<i>S. epidermidis</i>	11 (\pm 0.10)	14 (\pm 0.11)	17 (\pm 0.01)	19 (\pm 0.11)	25 (\pm 0.12)	28 (\pm 0.12)
<i>E. faecalis</i>	12 (\pm 0.11)	14 (\pm 0.11)	18 (\pm 0.12)	20 (\pm 0.12)	24 (\pm 0.12)	28 (\pm 0.12)
<i>S. pyogenes</i>	10 (\pm 0.10)	12 (\pm 0.10)	16 (\pm 0.11)	20 (\pm 0.11)	26 (\pm 0.12)	30 (\pm 0.12)
<i>C. diphtheriae</i>	-	-	-	10 (\pm 0.10)	16 (\pm 0.11)	20 (\pm 0.11)
<i>P. aeruginosa</i>	10 (\pm 0.10)	14 (\pm 0.10)	17 (\pm 0.11)	21 (\pm 0.11)	23 (\pm 0.12)	28 (\pm 0.12)
<i>E. aerogenes</i>	13 (\pm 0.10)	16 (\pm 0.11)	20 (\pm 0.11)	22 (\pm 0.12)	24 (\pm 0.12)	28 (\pm 0.13)
<i>K. pneumoniae</i>	14 (\pm 0.11)	16 (\pm 0.11)	20 (\pm 0.12)	24 (\pm 0.12)	26 (\pm 0.15)	28 (\pm 0.14)
<i>S. typhi</i>	-	-	12 (\pm 0.10)	14 (\pm 0.11)	16 (\pm 0.11)	18 (\pm 0.11)

- = no activity

Zone of inhibition = mm \pm SEM

Table 8: Antibacterial Effects of Moxi-Mo complex

Dilution ($\mu\text{g/ml}$)	0.19	0.38	0.77	1.55	3.125	6.25
Strains						
<i>S. aureus</i>	30 (\pm 0.16)	32 (\pm 0.16)	34 (\pm 0.13)	36 (\pm 0.16)	38 (\pm 0.16)	40 (\pm 0.17)
<i>S. epidermidis</i>	30 (\pm 0.12)	34 (\pm 0.13)	36 (\pm 0.13)	+	+	+
<i>E. faecalis</i>	36 (\pm 0.16)	38 (\pm 0.16)	40 (\pm 0.17)	+	+	+
<i>S. pyogenes</i>	14 (\pm 0.11)	18 (\pm 0.11)	24 (\pm 0.11)	28 (\pm 0.12)	30 (\pm 0.12)	32 (\pm 0.16)
<i>C. diphtheriae</i>	34 (\pm 0.13)	36 (\pm 0.16)	38 (\pm 0.16)	40 (\pm 0.17)	+	+
<i>P. aeruginosa</i>	24 (\pm 0.12)	26 (\pm 0.12)	28 (\pm 0.12)	30 (\pm 0.13)	32 (\pm 0.13)	34 (\pm 0.12)
<i>E. aerogenes</i>	22 (\pm 0.14)	24 (\pm 0.14)	26 (\pm 0.15)	30 (\pm 0.15)	34 (\pm 0.13)	36 (\pm 0.16)
<i>K. pneumoniae</i>	22 (\pm 0.11)	24 (\pm 0.11)	26 (\pm 0.12)	30 (\pm 0.12)	32 (\pm 0.13)	36 (\pm 0.16)
<i>S. typhi</i>	14 (\pm 0.11)	16 (\pm 0.12)	18 (\pm 0.13)	20 (\pm 0.14)	22 (\pm 0.14)	24 (\pm 0.14)

+ = no growth

Table 9. The order of antibacterial effectiveness of Moxi-metal complexes

Stains	Metal moxifloxacin complex strength
<i>S. aureus</i>	Mo> Cd > Mg > Cu.
<i>S. epidermidis</i>	Mo> Cd > Cu > Mg.
<i>E. faecalis</i>	Mo> Cd > Mg = Cu.
<i>S. pyogenes</i>	Mo = Cd = Cu > Mg.
<i>C. diphtheriae</i>	Mo> Cu > Mg > Cd.
<i>P. aeruginosa</i>	Mo> Mg > Cu > Cd.
<i>E. aerogenes</i>	Mo> Mg = Cu > Cd.
<i>K. pneumonia</i>	Mo> Mg > Cd > Cu.
<i>S. typhi</i>	Mo = Cu > Cd = Mg.

Table 10. Antioxidant potentials of Moxi-metal complexes

S.No.	Code	IC ₅₀ ±SEM ^a (µg/ml)
1.	Moxi-Cd	2.45 ± 0.25
2.	Moxi-Cu	19.73 ± 0.932
3.	Moxi-Mg	3.62 ± 0.19
4.	Moxi-Mo	3.01 ± 0.37
5.	Moxi	121 ± 2.31
6.	Standard	1.65 ± 0.16

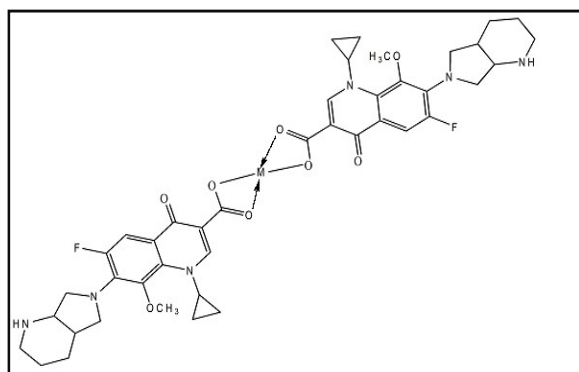


Figure 1. Structure of Moxi-metal complex

DISCUSSION

This study investigated antibacterial and antioxidant capabilities of Moxi-metal derivatives of Dihydroquinoline-3- carboxylate. All metal derivatives of Dihydroquinoline-3-carboxylate showed antibacterial activity compared to parent compound (Table 4-8). Antioxidant activity of metal derivatives was also higher, in table. 10 result of antioxidant effects of metal complexes of moxifloxacin in the form of IC₅₀ values are mentioned. The Moxi-metal complexes exhibited striking broad spectrum antibacterial activity against most of the organisms tested, as shown in Table 5-8. The study indicated that, although all compounds were effective, but Moxi-Mo and Moxi-Cd complexes showed extremely high antibacterial effect and proved superior over Moxi-Cu and Moxi-Mg metal complexes. These results suggest that metal conjugated drug delivery system makes drug to penetrate through effective route into bacteria thus inhibiting its growth and propagation. Multidrug resistant bacteria are continuously emerging due to inappropriate use of antibiotics resulting in lesser treatment options. The compound studied in this study are very strong candidates to be new therapy options. The substitution with metal groups in the carbonyl group and the presence of diverse metal ions make the scavenging effect possible. The synthesized Moxi-metal complexes showed almost similar or equal antioxidant effect comparable with standard ascorbic acid and they showed more potent antioxidant effects if compared to parent drug.

CONCLUSION

In this study Moxi-metal complexes of Cd, Cu, Mg and Mo were synthesized which were chemically attached to parent compound via carboxylate group and were ascertained bidentate. All metal complexes, synthesized in this study, have proved to be strong antibacterial compounds against gram-negative and gram-positive bacteria particularly against *S.typhi*, *P. aeruginosa* and *C.diphtheriae* to which parent compound Moxifloxacin was ineffective. The moxi-Mo and moxi-Cd complexes were more effective compared to moxi-Cu & moxi-Mg complexes. The prepared metal complexes exhibited almost similar or equal antioxidant activities compared to standard ascorbic acid and they showed more potent antioxidant effects compared to parent drug.

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