Medicinal chemistry

Danish et al., Med chem 2015, 5:8
http://dx.doi.org/10.4172/2161-0444.1000288

Research Article Open Access

Metal Complexes and Organotin(IV) Compounds of Cefixime and their Biological Study

Muhammad Danish[1]*, Muhammad Asam Raza[1]*, Tooba Ilyas[1], Amina Sharif[1] and Nargis Anjum[2]

[1]Department of Chemistry, University of Gujrat, Hafiz Hayat Campus, Gujrat, Pakistan
[2]Department of Chemistry, University of Sargodha, Sargodha, Pakistan

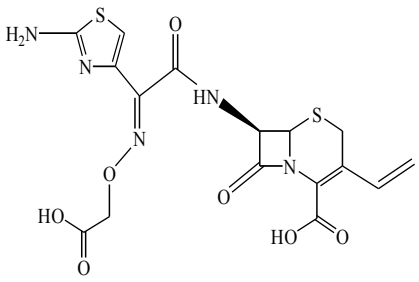
Abstract

Synthetic chemistry is playing revolutionary role in human beings by synthesizing novel compounds by different techniques. The present study was designed to prepare bioactive compounds and evaluate their antioxidant and enzyme inhibition studies. Metal complexes of cefixime were prepared by reacting metal salts of different transition metals with sodium salt of cefixime. Their characterization was done with melting point and FTIR studies which confirmed the synthesis of metal complexes. It was concluded from results that synthesized compounds showed very weak response against AChE and some extent to BChE. In contrast to esterase family protease was inhibited significantly and T4 exhibited more than 90% inhibition (93.2 ± 0.1%). Antioxidant study was conducted using well known DPPH free radical assay while enzyme inhibition potential was evaluated according to standard protocols. Maximum antiradical activity was exhibited by T6 (80.84 ± 1.6%) with IC_{50} 45 ± 2 µg/ml while T5 remained almost inactive. Antibacterial studies have been carried out against *Escherichia coli* and *Bacillus subtilis*.

Keywords: Metal complexes; Cefixime; DPPH, Proteases; AChE; BChE

Introduction

Cefixime has broad spectrum of activity, used mostly orally, high stability against β-lactamases and is susceptible to many organisms. Chemically, it is (*6R,7R*)-7-[2-(2-Amino-4-thia-zolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2- carboxylic acid, 7^2-(Z)-[O-(carboxymethyl) oxime] trihydrate.

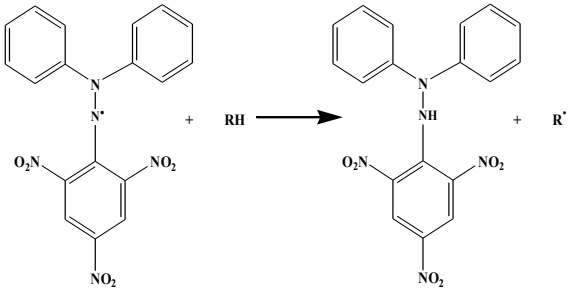


Cefixime

Cefixime like other cephalosporins inhibits the synthesis of bacterial cell wall which is the important cellular structure that strengthens the bacterial body and keep them safe from environmental hazards. It is efficiently used against number of bacteria including *Streptococcus pneumoniae, Staphylococcus aureus, Hemophilus influenzae, Moraxella catarrhalis, Streptococcus pyogenes, Escherichia coli, Klebsiella, Proteus mirabilis, Salmonella, Neisseria gonorrhoeae* and *Shigella*. It is used to treat otitis media, pharyngitis, bronchitis and urinary tract infections [1-4].

In biological systems, chain reactions can lead to severe damage or death of cells. Antioxidants act by inhibiting these chain reactions by trapping free radicals. Highly unstable free radicals and reactive oxygen species are present in living body from variety of sources. These free radicals may oxidize vital molecules of body like DNA, protein, lipids and nucleic acid leading body to degenerative diseases.

Antioxidants seem to protect body from chronic diseases including heart disease and cancer. Free radical scavenging activity was first reported by Miller et al [5].



DPPH DPPHH

Enzyme inhibitor is a organic chemical or inorganic metal or biosynthetic compound due to their covalent or non-covalent interactions with enzyme active site. They can reduce or completely inhibit the enzyme catalytic activity either reversibly or permanently (irreversibly) by modifying one amino acid, or several side chain(s) required in enzyme catalytic activity. In drug discovery, several drug analogues are chosen and/or designed to inhibit specific enzymes. Antibacterial substance is one of feed additives to be used in order to promote beneficial use of nutrient components in feed. Many authors are engaged now a days in preparation of metal complexes of some antibiotic in order to check potential of derivatives drugs [6-9]. Our research group is also working on such line to evaluate the comparability of the resistance in the bacterial and derivation. The aim of this study was to check the biological potential of metal complexes of Cefixime in terms of antibacterial, antioxidant and enzyme inhibition potential.

***Corresponding author:** Muhammad Danish and Muhammad Asam Raza, Department of Chemistry, University of Gujrat, Hafiz Hayat Campus, Gujrat, Pakistan, E-mail: asamgcu@yahoo.com; drdanish62@gmail.com

Received April 13, 2015; **Accepted** August 06, 2015; **Published** August 10, 2015

Citation: Danish M, Raza MA, Ilyas T, Sharif A, Anjum N (2015) Metal Complexes and Organotin(IV) Compounds of Cefixime and their Biological Study. Med chem 5: 373-377. doi: 10.4172/2161-0444.1000288

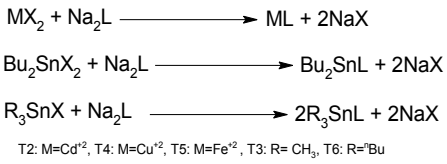
Experimental

Chemicals and instruments

DPPH (Diphenyl picryl hydrazyl), 5,5´-dithiobis [2-nitrobenzoic acid] (DTNB), protease and DMSO were purchased from Sigma-Aldrich (USA) while AChE (Acetylcholine esterase) and BChE (Butyrylcholine esterase) were obtained from Biochemistry Laboratory Mayo Hospital Lahore. All other chemicals and solvents used were of analytical grade from Merck. UV/Vis. Spectrophotometer (UV-4000, Shimadzu), atomic absorption spectrophotometer (Shimadzu, AA-6300) and FTIR (Shimadzu, IR-Prestige-21) were used during studies.

Synthetic scheme

The targeted compounds were prepared according to literature method [10,11]. Complexes of transition metal were prepared by drop-wise addition of aqueous solution of sodium salt of cefixime to an aqueous solution of transition metal salt (copper (II) chloride, cadmium (II) nitrate and iron (II) sulphate) in a 250 ml round bottom flask equipped with a water condenser and magnetic stirring bar. The reflux was carried out for about 3 hr till complete precipitation occurred. After the formation of precipitates, the reaction mixture was cooled, filtered and the residue was dried completely. Complexes of organotin halides with sodium salt of ligand acid were prepared by the addition of appropriate triorganotin chloride in methanol to the reaction mixture drop-wise with constant stirring. The reaction mixture was then refluxed for 4-6 hr, cooled and filtered. The filtrate was concentrated on rotary evaporator and then kept for crystallization. Recrystalization was carried out from a suitable solvent.



Synthetic Scheme

Characterization

Characterization of synthesized compounds were done with the help of UV/Vis and FTIR techniques while metal to ligand ration was calculated with atomic absorption spectrophotometer. In the spectrum mode of UV/Vis spectrophotometer, λ_{max} was determined. Blank solution was used to correct base line in the range of 190 nm-800 nm. Then sample cell was filled with very dilute sample solution and scan was obtained for UV/Vis spectrum (plot of wavelength vs absorbance). λ_{max} was detected from the peak maximum of the spectrum [12].

Antibacterial studies

The representative samples were individually tested against two bacterial strains including *Escherichia coli* and *Bacillus subtilis* using agar well diffusion method. Bacterial strains were available and maintained in the Microbiology laboratory, Department of Zoology, University of Gujrat, Gujrat. Strains were cultured overnight at 37 °C in nutrient agar medium [13].

Antioxidant activity

The radical scavenging ability was measured by using the method of Shahwar et al. [14]. 100 µl of the synthesized compound (5 mg/ml in DMSO) was added into 2 ml methanolic solution of DPPH. The reaction mixture was incubated at room temperature for 30 minutes. The decrease in absorbance at 517 nm was noted after 30 min.

The % age scavenging of radical was determined by the following formula.

$$\%\text{ age Inhibition of DPPH} = \frac{A - B}{A} \times 100$$

Where A is the optical density of blank and B is the optical density of sample.

Protease inhibition assay

Protease inhibition assay was carried out according to the method of Jedinak et al. with some modification [15]. Tris buffer (100 mM) of pH 7.5 was prepared by dissolving 12.1 g of tris (hydroxymethyl)-aminomethane in distilled water and adjusted pH 7.5 with HCl (5 M). The stock solution of trypsin was prepared by dissolving 2 mg of trypsin in 10 ml of 1.0 mM HCl. Nα-benzoyl-DL-arginine-paranitroanilide hydrochloride (BApNA) was dissolved in DMSO (20 mg/ml). Enzyme (0.3 ml) and inhibitor (100 µl) was incubated at 37 °C for 15 minutes then 0.6 mM substrate was added and final volume was made 2.5 ml with tris buffer. The reaction mixture was incubated at 37 °C for 30 minutes. The reaction was quenched by adding 30% acetic acid (0.1 ml) and read the absorbance at 410 nm using UV/Vis spectrophotometer.

The percentage inhibition was calculated by using the following formula;

$$\%\text{ Inhibition} = \frac{\text{Absorbance (blank) - Absorbance (test)}}{\text{Absorbance (blank)}} \times 100$$

Acetylcholine/Butyrylcholine esterase assay

Acetyl/butrylcholine esterase inhibitory activity was measured by spectrophotometric method of Abbasi et al. [16]. Acetyl/butyrylthiocholine iodide was used as substrate in the assay. The reaction mixture contained 1500 µl of (100 mM) tris buffer (pH 7.8), 100 µl of DTNB, 100 µl (5 mg/ml) of test compound solution and 100 µl of enzyme, which were mixed and incubated for 15 min (37 °C). The reaction was initiated by the addition of 100 µl acetyl/butyrylthiocholine iodide. The hydrolysis of acetyl/butrylthiocholine iodide was monitored at 412 nm after 30 min. All the reactions were performed in triplicate. The percentage inhibition was calculated as follows:

$$\%\text{ age Inhibition} = \frac{E - S}{E} \times 100$$

Where E is the activity of the enzyme without test compound and S is the activity of enzyme with test compound.

Results and Discussion

Characterization

The infrared studies of the complexes show that this drug has donor atoms that can bind to metal ions forming multinuclear chelates. It bonds to metal ion through the carboxylate ion, the nitrogen of the *β*-lactam thiozolidine ring and oxygen atom of lactam C=O group rather than amide carbonyl group [17].

In the spectrum mode of UV/Vis spectrophotometer, λ_{max} was determined. The value of λ_{max} for ligands understudy and synthesized complexs are presented in Table 1. The value of λ_{max} for all the compounds was found between 291-298 nm that indicated the presence of various chromophoric groups (C=O, C=C, C=N) in current study. The unsaturation of these groups is responsible for $\pi \rightarrow \pi^*$ transitions. The close resemblance in the λ_{max} values of ligand and complexes showed that chromophoric groups are similar in both the cases. According to Woodward-Fisher rule the contribution of unsaturated groups (C=O, C=C, C=N) towards the λ_{max} is also in the favor of complexation. A very little difference in λ_{max} values of complexes from that of ligand

may arise due to the co-ordination of the ligand with metal ions to form complexes.

The infrared spectra of the ligands and prepared compounds were recorded as KBr pellets in the range 4000–400 cm^{-1}. FTIR absorptions of these complexes were assigned in comparison with that of free acids and their sodium salts. IR absorptions of those wave numbers are discussed mainly here which are directly involved in complex formation. The absorption bands were assigned by comparison with earlier reports [18] and important frequencies such as $\nu(CO)_{lactam}$, $\nu(C=O)$-NH, $\nu(COO)_{asym}$, $\nu(COO)_{sym}$ and ν(Sn-O) are listed in Table 2. The broad band at 2730-2980 cm^{-1} due to ν(OH) present in the spectrum of the ligand is absent in the spectra of corresponding synthesized complexes thus showing complex formation.

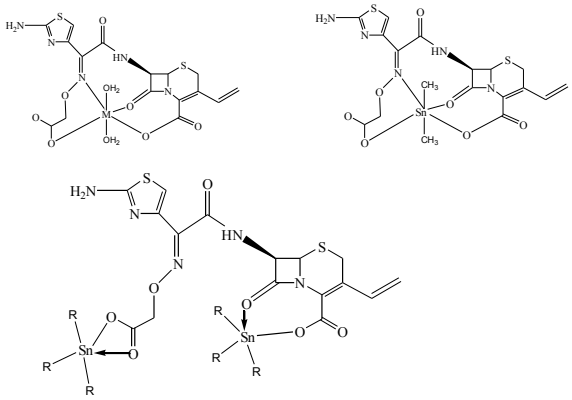
After complexation, the C = O of carboxylic acid shifts between 1660-1539 cm^{-1} as compared to free acid at 1670 cm^{-1}. Similarly, coordination of β-lactam of carbonyl group takes place as compared to ligand and sodium salt hence C = O double bond character decreases and this vibration shifts to lower region between 1770-1730 cm^{-1}.

Values of group $\nu(COO)_{asym}$ vibrations lowered due to presence of delocalization of π-electrons in the adjacent C=C and C=O bonds, this delocalization increases single band character in them hence lowers the frequencies of C=O and C=C groups.

The lactam ν(CO) band appears in range of 1774-1770 cm^{-1} in free acids and their sodium salts while in spectra of complexes this bond is shifted to lower absorptions indicating that bonding occurs through the oxygen atom of lactam C=O group. The asymmetric stretching absorptions of carboxylate group and lactam group are decreased depending on the nature of metal ion. The shifting of absorptions due to amide carbonyl bond $\nu(C=O)$-NH in complexes is not remarkable in comparison to free acid and its salt thus indicating that ligand coordination with metal ions takes place through oxygen atom of lactam C=O group rather than amide carbonyl group [19]. In case of respective organotin(IV) complexes, absorptions due to Sn-O band are recorded in the range of 500-400 cm^{-1}.

The IR studies of cefixime ligand and its respective complexes suggested that this antibiotic has number of donar atoms that can bind to the metal ions forming multinuclear chelates.

In order to ascertain about the geometry of these amorphous compounds, metal to ligand ratio was determined using atomic absorption spectrophotometry and results are shown as in the Table 1. These results show that in case of transition metal complex as well as diorganotin(IV) complex, metal to ligand ratio is 1:1, thus showing distorted octahedral geometry. However, in case of triorganotin complexes metal to ligand ratio is 2:1 which shows that each carboxylate group consumes one organotin moiety resulting in distorted trigonal bipyramidal geometry. It is, however, pertinent to mention that in absence of a clear cut X-ray report geometry of these complexes can not be ascertained and literature is also scarce about such systems.



T2: M=Cd^{+2}, T4: M=Cu^{+2}, T5: M=Fe^{+2}, T3: R=CH_3, T6: R=^{n}Bu

Proposed structures of the complexes

Microbiological screening

Size of inhibition diameter was measured to determine the susceptibility of strains of bacterium towards cefixime and their representative metal complexes. During biological testing the complexes remain intact as assessed by color. Bactericide diameter measured for ligands and complexes shows that they have good activity as bactericide as shown in Table 3.

The results have shown that the metal complexes have two types of behaviour compared with ligands against the same bacteria and under the identical experimental conditions. For example, some of metal complexes show higher bactericidal activity than that of corresponding ligand and some complexes have less activity than ligand. These differences may arise due to steric, electronic, pharmacokinetic factors along with mechanistic pathways.

Protease, AChE and BChE inhibition activity

All synthesized compounds were screened against available enzymes (Protease, AChE and BChE). Interesting results were obtained during this study. About all complexes showed significant activity. Among them T4 (CuL) exhibited maximum activity (93.2 ± 0.1%) with IC_{50} 78 ± 1 µg/ml for protease as shown in Table 4 and Figure 1. During this evaluation it was found that ligand remained almost inactive but its complexes has greater activity than ligands, which showed that metal ion has changed the configuration of cefixime antibiotic for binding to active sites of enzyme.

These complexes along their ligand were also evaluated in terms of AChE and BChE inhibition studies. It was observed that very low response was exhibited by all complexes against AChE and same behavior was observed for BChE except T2 (CdL). These results indicated that these agents have very low potential to inhibit the active site of enzyme. Enzyme inhibition play vital role in curing various diseases in human beings. Extensive research on this topic is being

Compound	Code	color	State	Solubility	Yield (%)	m.p (°C)	λmax (nm)	M:L ratio
Ligand	T1	Yellowish	Powder	C_2H_5OH	-	220	291	-
CdL	T2	Green	Powder	C_2H_5OH	83	240	297	1:1
$(Me)_3SnL$	T3	Brown	Powder	C_2H_5OH	75	167	195	2:1
CuL	T4	Brown	Powder	C_2H_5OH	74	363	196	1:1
FeL	T5	Brown	Powder	C_2H_5OH	62	340	197	1:1
$(Bu)_3SnL$	T6	Brown	Powder	C_2H_5OH	70	158	197	2:1
$(Bu)_2SnL$	T7	Brown	Powder	C_2H_5OH	74	167	196	1:1

Table 1: Physical properties, λmax values and metal to ligand ration of the ligand/complexes.

carried on and it is reported in literature that metal complexes of quinolone enhance the antimicrobial activity of drug [20].

Antioxidant activity

Oxidative reactions are necessary for maintenance of life but they may cause damage by producing ROS or highly unstable free radicals. Antioxidants seem to protect body from damage caused by free radicals and ROS, by trapping these unstable moieties. As their higher concentration increase the risk of CHD and many other disorders. Antioxidant activity of synthesized compounds was checked by using well reported stable free radical DPPH. All compounds showed remarkable activity except T3 [$(Me)_3SnL$] and T5 (FeL) which almost remained inactive. It was also concluded that there is small difference between activity of ligand and their metal complexes. Maximum activity (80.84 ± 1.6%) was exhibited by T6 [$(Bu)_3SnL$] with IC_{50} value 45 ± 2 µg/ml (Table 5 and Figures 2 and 3). The order of potential of compounds in antiradical scavenging activity is: T6>T7>T4>T2>T1>T3>T5. Our results suggest that these compounds can be used as antioxidant.

Compounds	Code	β lactam *v*(C=O) cm^{-1}	*v*(HNC=O) cm^{-1}	*v*(COO)asym cm^{-1}	*v*(COO)sym cm^{-1}	*v*(C-O) cm^{-1}	*v*(Sn-O) cm^{-1}
Ligand	T1	1774	1587	1660	1410	1030	-
Na_2L	-	1770	1593	1668	1417	1035	-
CdL	T2	1768	1535	1680	1377	1045	-
$(Me)_3SnL$	T3	1720	1532	1620	1314	1010	417
CuL	T4	1741	1535	1678	1311	1060	-
FeL	T5	1755	1539	1672	1421	1002	-
$(Bu)_3SnL$	T6	1703	1336	1539	1406	1055	459
$(Bu)_2SnL$	T7	1766	1535	1589	1319	1053	450

Table 2: Fundamental IR vibrations of the cefixime complexes.

Compound	Zone of inhibition E.C. (mm)	Zone of inhibition B.S. (mm)
Ligand	13-24 (H.A)	11-12 (M.A)
T2	15-29 (H.A)	15-16 (M.A)
T3	11-29 (H.A)	02-06 (M.A)
T4	09-27 (H.A)	09-21 (M.A)
T5	10-24 (H.A)	10-15 (M.A)
T6	06-25 (H.A)	07-25 (M.A)
T7	15-21 (H.A)	12-18 (M.A)

*E.C. *Escherichia coli,* B.S. *Bacillus subtilis*
*H.A: Highly active, M.A: Moderatly active, L.A: Less active

Table 3: Antibacterial activities of the ligand and complexes.

		Enzyme inhibition					
Sample	Code	Protease	IC50 (µg/ml)	AChE	IC_{50} (µg/ml)	BChE	IC50 (µg/ml)
Ligand	T1	64.4 ± 0.7	153 ± 2	9.9 ± 0.1	-	26.84 ± 0.2	-
CdL	T2	62.6 ± 0.4	197 ± 2	3.3 ± 0.3	-	57.40 ± 0.3	210 ± 2
$(Me)_3SnL$	T3	60.5 ± 0.3	205 ± 1	12.7 ± 0.3	-	22.78 ± 0.4	-
CuL	T4	93.2 ± 0.1	78 ± 1	3.1 ± 0.5	-	13.17 ± 0.6	-
FeL	T5	28.1 ± 0.5	-	5.8 ± 0.2	-	24.84 ± 0.2	-
$(Bu)_3SnL$	T6	59.0 ± 0.2	210 ± 3	11.4 ± 0.1	-	17.91 ± 0.3	-
$(Bu)_2SnL$	T7	44.9 ± 0.6	-	30.7 ± 0.4	-	19.28 ± 0.5	-

** 100 µl samples (5 mg/ ml DMSO), - = Not Calculated*

Table 4: Enzyme inhibition activity.

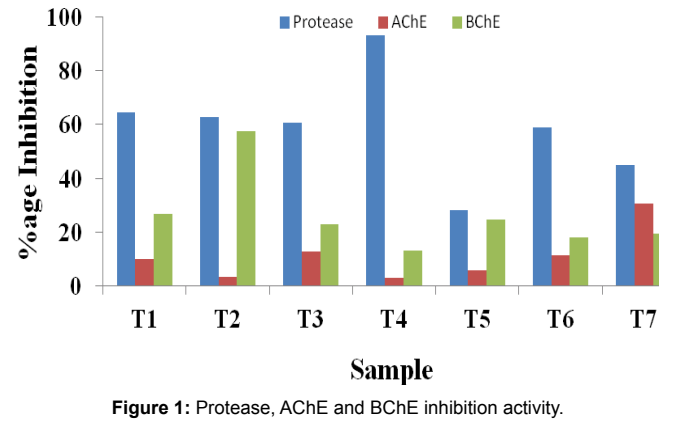


Figure 1: Protease, AChE and BChE inhibition activity.

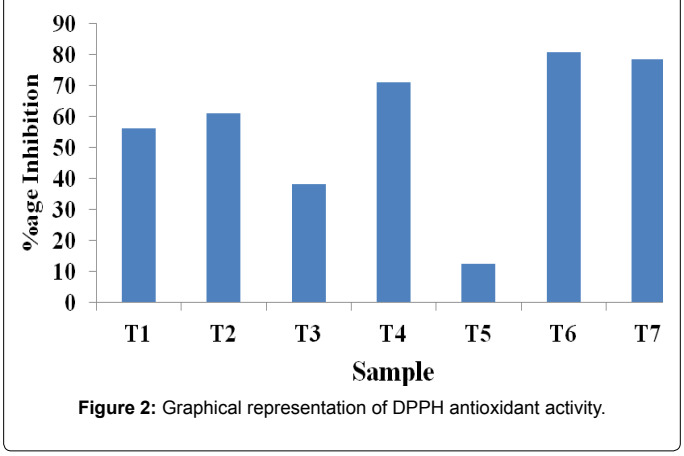


Figure 2: Graphical representation of DPPH antioxidant activity.

	DPPH Activity		
Sample	**Code**	**%age Inhibition**	**IC50 (µg/ml)**
Ligand	T1	56.21 ± 1.1	49 ± 2
CdL	T2	61.05 ± 1.3	80 ± 3
$(Me)_3SnL$	T3	38.12 ± 1.0	-
CuL	T4	71.10 ± 1.4	46 ± 1
FeL	T5	12.63 ± 1.3	-
$(Bu)_3SnL$	T6	80.84 ± 1.6	45 ± 2
$(Bu)_2SnL$	T7	78.37 ± 1.7	49 ± 3

** 100 µl samples (5 mg/ ml DMSO), - = not calculated*

Table 5: DPPH antioxidant activity.

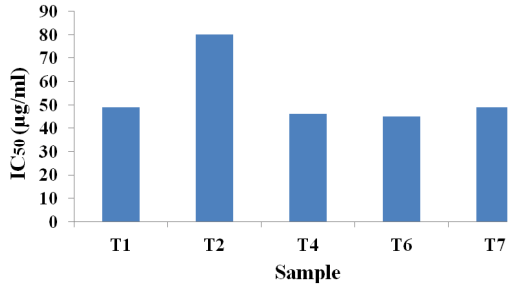


Figure 3: Graphical representation IC_{50} values of synthesized compounds.

Conclusion

In modern era with the development of coordination chemistry, it is accepted that complexes not only increase drug efficiency but also enhance its effectiveness against particular disease as compared to simple drug. These complexes were found more active as compared to the simple ligand against various microbes. Similarly, these possess more antioxidant potential than that of drug alone. Furthermore, these metal complexes are good protease inhibitors and showed moderate response against AChE as well as BChE. This study suggested that these bioactive metal complexes may be used as free radical scavengers as well as antimicrobial agents.

References

1. Wenzel U, Gebert I, Weintraut H, Weber WM, Clauss W, et al. (1996) Transport characteristics of differently charged cephalosporin antibiotics in oocytes expressing the cloned intestinal peptide transporter PepT1 and in human intestinal Caco-2 cells. J Pharmacol Exp Ther 277: 831-839.
2. Glahn RP, Van Campen DR (1997) Iron uptake is enhanced in Caco-2 cell monolayers by cysteine and reduced cysteinyl glycine. J Nutr 127: 642-647.
3. Steinhardt HJ, Adibi SA (1984) Interaction between transport of zinc and other solutes in human intestine. Am J Physiol 247: G176-182.
4. Brown DH, Smith WE, Teape JW, Lewis AJ (1980) Antiinflammatory effects of some copper complexes. J Med Chem 23: 729-734.
5. Miller HE, Rigelhof F, Marquart L, Prakash A, Kanter M (2000) Whole-grain products and antioxidants. Cereal Food World 45: 59-63.
6. Pillai SM, Pushpa LS (2012) Designing of some novel metallo antibiotics tuning biochemical behavior towards therapeutics: Synthesis, characterisation and pharmacological studies of metal complexes of cefixime. J Saudi Chem Soc.
7. Juan R, Anacona, Jesus Estacio JE (2006) Synthesis and Antibacterial Activity of Cefixime Metal Complexes. Transition Metal Chemistry Chem 3: 227-231.
8. Arayne MS, Sultana N, Khanum F, Ali MA (2002) Antibacterial studies of cefixime copper, zinc and cadmium complexes. Pak J Pharm Sci 15: 1-8.
9. Abdul AR, Hasna M, Marwa D (2013) Novel formation three complexes of cefixime-copper using acetate-acetic acid buffer and determination of cefixime in pure and pharmaceutical dosage forms. Int J Pharm Pharm Sci 5: Suppl 469-477.
10. Ahmad MS, Hussain M, Hanif M, Ali S, Qayyum M, et al. (2008) Di- and triorganotin(IV) esters of 3,4-methylenedioxyphenylpropenoic acid: synthesis, spectroscopic characterization and biological screening for antimicrobial, cytotoxic and antitumor activities. Chem Biol Drug Des 71: 568-576.
11. Jabbar S, Shahzadi I, Rehman R, Iqbal I, Qurat-Ul-Ain, et al. (2012) Synthesis, characterization, semi-empirical study, and biological activities of organotin(IV) complexes with cyclohexylcarbamodithioic acid as biological active ligand. J Coord Chem 65: 572-590.
12. Loon J (1985) Biological and Environmental Samples; Jon Wiley and Sons: New York, 28-36.
13. Shahwar D, Raza MA, Tariq S, Riasat M, Ajaib M (2012) Enzyme inhibition, antioxidant and antibacterial potential of vasicine isolated from Adhatoda vasica Nees. Pak J Pharm Sci 25: 651-656.
14. Shahwar D, Rehman SU, Raza MA (2010) Acetyl cholinesterase inhibition potential and antioxidant activities of ferulic acid isolated from Impatiens bicolor Linn. J Med Plants Res 4: 260-266.
15. JedinÃ¡k A, Maliar T, Grancai D, Nagy M (2006) Inhibition activities of natural products on serine proteases. Phytother Res 20: 214-217.
16. Shahwar D, Raza MA, Mirza ASM, Abbasi MA, Ahmad VU (2010) Comparative study of antioxidant and antimicrobial activities of stem-bark extracts of Litchi chinensis and its organic fractions. J Chem Soc Pak 32: 357-362.
17. Auda SH, Mrestani Y, Fetouh MI, Neubert RH (2008) Characterization and activity of cephalosporin metal complexes. Pharmazie 63: 555-561.
18. Hamm P, Lim M, Hochstrasser M (1998) Structure of the Amide I Band of Peptides Measured by Femtosecond Nonlinear-Infrared Spectroscopy. J Phys Chem 102: 6123-6138.
19. Abo El-Maali N, Osman AH, Aly AA, Al-Hazmi GA (2005) Voltammetric analysis of Cu (II), Cd (II) and Zn (II) complexes and their cyclic voltammetry with several cephalosporin antibiotics. Bioelectrochemistry 65: 95-104.
20. Uivarosi V (2013) Metal complexes of quinolone antibiotics and their applications: an update. Molecules 18: 11153-11197.

Citation: Danish M, Raza MA, Ilyas T, Sharif A, Anjum N (2015) Metal Complexes and Organotin(IV) Compounds of Cefixime and their Biological Study. Med chem 5: 373-377. doi: 10.4172/2161-0444.1000288