*Journal of Pharmaceutical Research International*

***Volume 35, Issue 2, Page 30-40, 2023; Article no.JPRI.97044***
***ISSN: 2456-9119***
*(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)*

# Infrared Spectroscopic Study of Binding Interaction of Metal Complexes with Mefenamic Acid (MFA)

**Md. Aminul Hoque [a++], Anan Mahabub Aboni [a++], Tasbira Jasmeen [a#] and Sherejad Sanam [a†*]**

*[a] Department of Pharmacy, Stamford University Bangladesh, Dhaka, Bangladesh.*

***Authors' contributions***

*This work was carried out in collaboration among all the authors. Author SS designed the study, supervised the whole research work and contribute in data analysis. Authors MAH and AMA are the principal researchers who performed all laboratory work following the protocol. Author AMA has performed the statistical analysis, wrote the draft copy of the manuscript and searched the literatures. All authors read and approved the final manuscript.*

***Article Information***

DOI: 10.9734/JPRI/2023/v35i27313

**Open Peer Review History:**
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/97044

***Original Research Article***

***Received: 02/01/2023***
***Accepted: 28/02/2023***
***Published: 04/03/2023***

## ABSTRACT

**Aims:** The foremost aim of this study was to evaluate the 1:1 formed complex when mefenamic acid interacts with $Cu^{2+}$, $Zn^{2+}$, and $EDTA^{4-}$ metal at the physiological condition, which provides a better understanding of the pharmacological studies. This research provided information on the binding affinity of mefenamic acid with selective metals. It helps with preparative, structural, and reactivity studies for multiple drug designs in pharmaceutical fields.
**Place and Duration of Study:** Department of Pharmacy, Stamford University Bangladesh, Dhaka, Bangladesh & CARS ((Centre for Advanced Research in Sciences), University of Dhaka. The duration of this study is between September to December 2022.

*[++] Student, Bachelor of Pharmacy (Honor's);*
*[#] Chairman;*
*[†] Assistant Professor;*
**Corresponding author: E-mail: sherejadsanam@stamforduniversity.edu.bd;*

**Study Design:** The Infrared spectra of Copper (Cu), Zinc (Zn), and Ethylenediaminetetraacetic Acid (EDTA) complex of Mefenamic Acid were investigated in the region between 4000 and 400 $cm^{-1}$. These spectra were compared to standard peaks with specific functional groups. The binding interactions of the selected metal ions were demonstrated by significant variations in the intensities of the amino group of mefenamic acid after metal complexation.
**Results:** The interactions of the metal ions with the acid product have resulted in the alteration of the functional structure, characterized by a negligible reduction in the structure of mefenamic acid. The change in position of the characteristic bands, or the increase/ decrease in the number of bands and appearance of a new metal-atom bond, helps to confirm the formation of a complex.
**Conclusion:** It has been recently found that metal-based complexes decrease antiviral, antibacterial, and anticancer action. In order to construct actively functioning medications, it is vital to study the ability of physiologically active metal ions to interact with metalloproteinases like albumin, which transport and distribute these metal ions. The current research set a standard for repeatable mefenamic acid metal ion research.

*Keywords: Mefenamic acid; infrared spectroscopy; FT-IR; binding interactions; metal complexation; amino group; copper; zinc; EDTA; functional structure.*

## ABBREVIATIONS

*MFA : MEfenamic Acid*
*Cox 1 : Cyclooxygenase 1*
*Cox 2 : Cyclooxygenase 2*
*pge 2 : Prostaglandin e2*
*Edta : Ethylenediaminetetraacetic Acid*
*NSAID : Nonsteroidal Anti-Inflammatory Drug*
*GI : Gastro Intestinal*
*GABA : Gamma-Aminobutyric Acid*
*MCT : Mercury Cadmium-Telluride*
*FT-IR : Fourier Transform Infrared*

## 1. INTRODUCTION

Mefenamic acid and its metal-binding derivatives, many of which function by chelation, have produced effective medications and selective toxins. They have various medical purposes [1]. Inorganic and medicinal chemistry studies metal complexes with active drugs as ligands to develop new drugs. NSAIDs are a prominent ligand for metal complex synthesis [2].

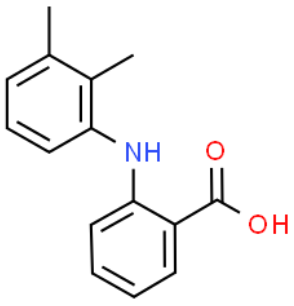



**Fig. 1. Structure of mefenamic acid**

Mefenamic acid is a nonsteroidal anti-inflammatory agent—a non-selective inhibitor of COX-1 and COX-2. Mefenamic acid has a limited anti-inflammatory effect in humans despite being analgesic and antipyretic. Severe gastrointestinal side effects limit its use. It has a slight advantage over other NSAIDs. It is often prescribed for less than one week. 750–1500 mg is the daily human dosage. To reduce GI side effects, it should be taken with food [3].

Mefenamic acid's physiology is diverse. It inhibits protein and receptor binding sites. This removes thyroxine, uric acid, and warfarin from protein carriers [4]. It modulates the immunological system & inhibits platelet aggregation [5,6]. Mefenamic acid is neurotoxic but also neuroprotective [7,8]. GABA receptors are modulable and activatable [8]. Mefenamic acid inhibits pyrogens like other NSAIDs.

Mefenamic acid is weakly soluble in its acidic state. However, its sodium salt could make it significantly more soluble. The absorption rate of mefenamic acid after oral administration is up to 80%. 2–6 mg/L (250-mg dose) and 4–24 mg/L (500-mg dosage) peak blood levels are achieved in 2–4 h after taking the unconjugated drug [9]. Half-life is approximately 2–4 hours, and blood levels are below 0.1 mg/L after 24 hours.

Mefenamic acid is helpful for chronic pain of bone, muscle, neuropathy, and soft tissue diseases [10]. It has proved to be as effective as ibuprofen, naproxen, ketoprofen, piroxicam, etc [11,12] [13]. Mefenamic acid is superior to dextropropoxyphene and paracetamol [14]. According to a study, it is as effective or more

effective as other NSAIDs for chronic osteoarthritis patients [15,16].

Toxic effects are related to iodine consumption with mefenamic acid [17]. Consumption of 2,5-Dimethoxy-4-ethylamphetamine with mefenamic acid increases the risk or severity of hypertension. 4-hydroxycoumarin with mefenamic acid exacerbates GI problems [18]. Mefenamic acid paired with Benazepril and enalapril can increase renal failure, hyperkalemia, and hypertension. Caffeine decreases its metabolism. Mefenamic acid with Cefprozil and Mannitol may induce nephrotoxicity. It may lower the elimination rate of Diazepam, digoxin, flurazepam, and folic acid, resulting in a higher serum level.

It is well known that transition metal complexes with nonsteroidal medicines are more efficacious and less toxic than their parent medications [19]. Divalent metal complexes with various NSAIDs are better anti-inflammatory options than NSAIDs because their structures interact more specifically with target enzymes [20]. Metal ions also boost antioxidant and anticancer action [21].

Our studies were stimulated by the fact that most anti-inflammatory drugs are carboxylic acids with their carboxylate group prone to metal binding [19,22]. Some of the complexes of mefenamic have been written about. Tapacli and Ide wrote about compounds of mefenamic that have Ca and Na ions [1]. Kovala-Demertzi and his colleagues looked into the compounds $SnPh_3$(mef) and $SnBu_2(mef)_2$ [2].

The present work aimed to obtain the mefenamate complexes of copper, zinc & EDTA & to gain a better comprehension of the pharmacological experiments. It is recently found that metal-based complexes decrease antiviral, antibacterial, and anticancer action. In order to construct actively functioning medications, it is vital to study the ability of physiologically active metal ions to interact with acid.

The therapeutic use of transition metal complexes is a relatively new field of study with a lot of potential for future development. There is a lack of fundamental principles to guide the synthesis and development of medications based on transition metals. Improvements in techniques like combinatorial chemistry will improve the production of inorganic molecules for use as pharmaceuticals. It is reasonable to assume that metal complexes' effects on complete organisms will be distinct from those of non-metal-containing substances and hence may provide novel possibilities for study, diagnosis, and treatment.

## 2. MATERIALS AND METHODS

### 2.1 Materials and Reagents

All chemicals and reagents were of analytical grade and were used as supplied, while the solvents were purified according to standard procedure. Mefenamic acid (99.1% purity) was obtained from ACI Pharmaceutical Co. Ltd. copper sulphate ($CuSO_4$), zinc sulphate ($ZnSO_4$), and EDTA (Ethylenediamine tetra acetic acid) was collected from Stamford University Bangladesh, pharmaceutical analysis laboratory. Ethanol & methanol were used for experimental purposes, which were of analytical grade.

### 2.2 FT-IR Spectroscopy Instrumentation and Conditions

FT-IR spectroscopy measurements were done using the IRTracer-100 (Shimadzu, Japan) under physiological conditions. The IRTracer-100 has a stable dynamic alignment mechanism and a high S/N ratio of 60,000:1 for highly sensitive and accurate measurements. Additional detectors, light sources, and beam splitters can be added to expand to the far-IR and near-IR ranges (12,500 to 240 $cm^1$) and to increase sensitivity with an MCT (Mercury Cadmium-Telluride) detector. The instrument can obtain up to 20 spectra/second for rapid reaction monitoring or in-line gas measurement. FT-IR works based on Michelson Interferometer, which has a beam splitter, fixed mirror, and moveable mirror.

### 2.3 Sample Preparation

#### 2.3.1 Synthesis of mefenamic acid with copper sulphate

A solution of copper (II) sulfate (0.567 mmol) methanol (2.0mL) was added to a solution of mefenamic acid (1.5 mmol) in methanol (2.0 mL), and a piece of magnet was taken in a round bottom flask. The reaction mixture was rotated by an Analog Hot Plate Magnetic Stirrer 120mm metal surface for up to 60 minutes at room temperature, and a blue powder was precipitated. The mixture was cooled to 5°C in a refrigerator for 4 hours. The primary purpose of

cooling a reaction is to settle down the precipitate completely. The precipitate was collected by filtration, washed with cold methanol\water to ensure the pure precipitate, and dry in vacuo to afford [2].

#### 2.3.2 Synthesis of mefenamic acid with zinc sulphate

A solution of zinc sulfate (0.50 mmol) methanol (2.0mL) was added to a solution of mefenamic acid (1.4mmol) in methanol (2.0 mL), and a piece of magnet was taken in a round bottom flask. The reaction mixture was rotated by an Analog Hot Plate Magnetic Stirrer 120mm metal surface for up to 60 minutes at room temperature, and a white powder was precipitated. The mixture was cooled to 5°C in a refrigerator for 4 hours. The main purpose of cooling a reaction is to completely settle the precipitate. The precipitate was collected by filtration, washed with cold methanol\water to ensure the pure precipitate, and dry in vacuo to afford [2].

#### 2.3.3 Synthesis of mefenamic acid with EDTA

A solution of EDTA (0.48 mmol) methanol (2.0mL) was added to a solution of mefenamic acid (1.4 mmol) in methanol (2.0 mL), and a piece of magnet was taken in a round bottom flask. Water totally dissolves EDTA. Therefore precipitate is infrequent. Methanol is soluble; thus, we combined a small amount of EDTA (0.48 mmol) with 1.4 mmol mefenamic acid to identify a trace level of interaction for further study. The reaction mixture was rotated by an Analog Hot Plate Magnetic Stirrer 120mm metal surface for up to 60 minutes at room temperature, and a blue powder was precipitated. The mixture was cooled to 5°C in a refrigerator for 4 hours. The main purpose of cooling a reaction is to settle down the precipitate completely. The precipitate was collected by filtration, washed with cold methanol\water to ensure the pure precipitate, and dry in vacuo to afford [2].

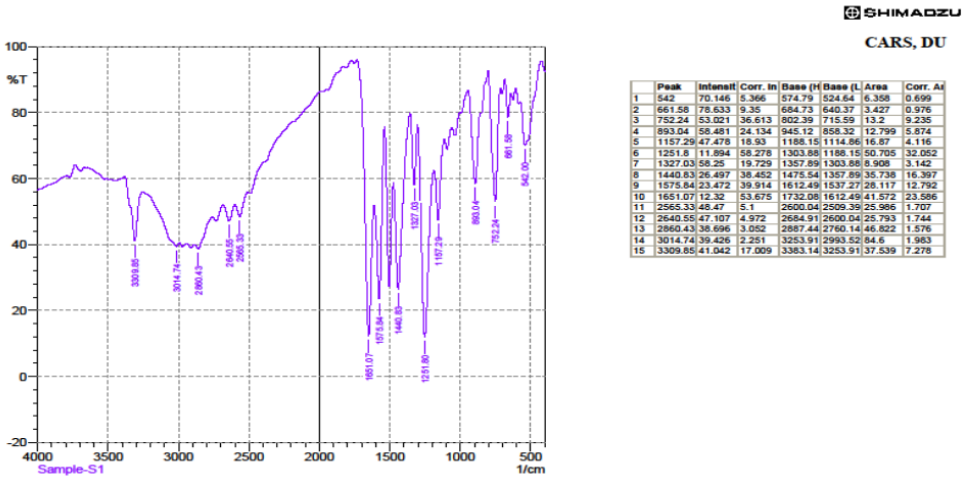
## 3. RESULTS AND DISCUSSION

FT-IR spectra were recorded to assess the compatibility of the drugs. FT-IR spectra for mefenamic acid, copper metal, zinc metal, EDTA, and the physical mixture of these drugs at the ratio of (1:1) were revealed by means of an FT-IR spectrophotometer using the instrument (FTIR). The scanning range was (400 to 4000) $cm^{-1}$. Mefenamic acid and metal-complex (1:1 ratio, w/w) mixture can be placed directly into the path of the infrared beam for each measurement. KBr pressed disk was used. A 1:1 mixture of drug and potassium bromide was weighted. Samples were mixed in a mortar and then pressed for 2-3 minutes to form a semitransparent pellet which lets light be transmitted to the detector.

As mefenamic acid is a weak acid, it must have a -COOH functional group. This study seeks complicated compounds with different functional groups. A band near 3500 $cm^{-1}$ (NH stretch.) was monitored only for mefenamic acid. The backbone conformation of the structure is directly related to the benzene ring, as 32000–2800 $cm^{-1}$, where sp C-H (stretching) and $sp^2$ C-H (stretching) were found. Also, we have the value of 1157.29 $cm^{-1}$, which indicates the presence of the C-O functional group. Finally, difference spectra were produced by adding metal ion complexes. These difference spectra monitored intensity changes upon complex formation. These structures of free drug and drug–metal ion complexes were studied, and the intensity of the corresponding functional group was calculated to measure complex formation. Peak intensity and area were calculated in the range of the drug's structural components. Mefenamic acid and metal ions interacted 1:1 at various concentrations.

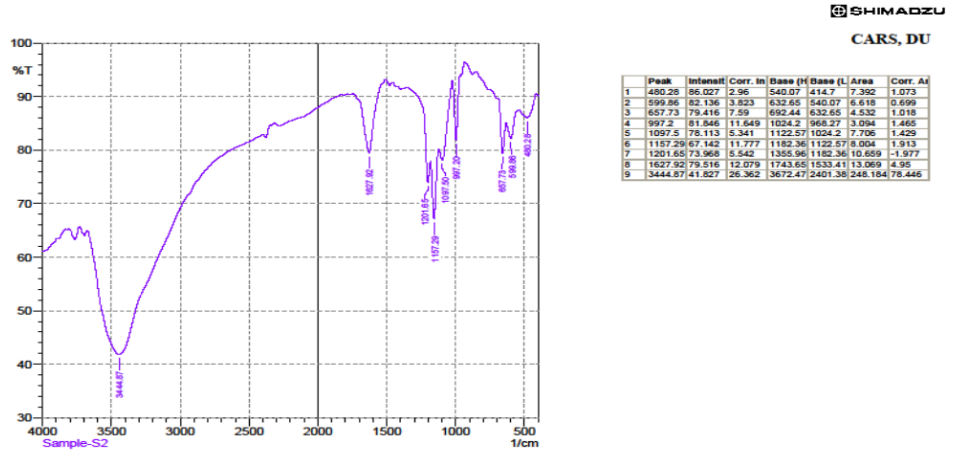
### 3.1 Individual Data of Selective Compounds

Interpretation of mefenamic acid and other metallic compounds were measured under the physiological condition as in Figs. (2 to 10). It was viewed that the raw sample of mefenamic acid was given a strong and broad peaks at 3309 $cm^{-1}$, 3014$cm^{-1}$, 2860$cm^{-1}$, and 2640 $cm^{-1}$ wavelength which indicated N-H, C=C, C-C groups (Fig. 2) respectively. The raw sample of copper sulphate was given strong and broad peaks at 3444 $cm^{-1}$ wavelength, which indicated the N-H group (Fig. 3). Zinc sulphate gives a strong and broad peak at 3564 $cm^{-1}$ and indicates O-H groups (Fig. 4). Finally, were measured the interpretation of mefenamic acid with copper sulphate, zinc sulphate, and EDTA, respectively at 3430 $cm^{-1}$, 3444$cm^{-1}$, and 3516 $cm^{-1}$ and indicated N-H and O-H bond formed by $sp^3$ hybridization (Figs. 5-7).



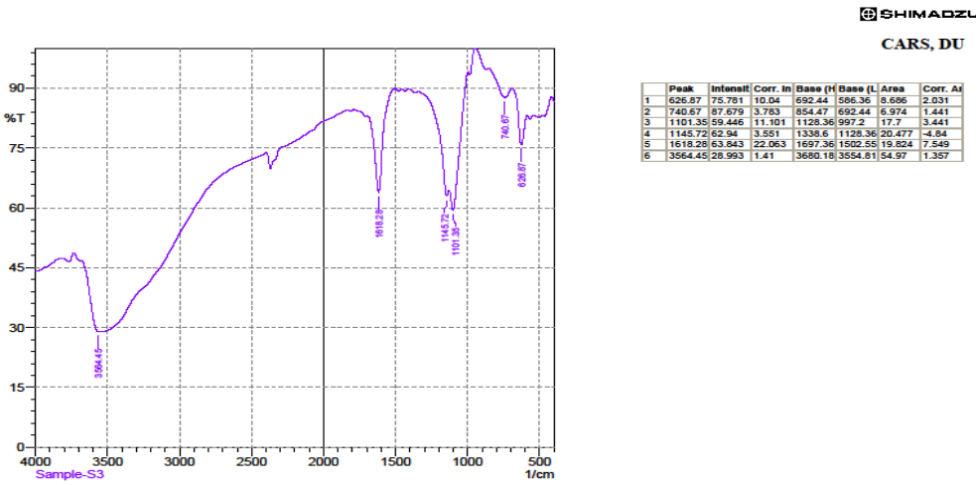

| | Peak | Intensit | Corr. In | Base (H | Base (L | Area | Corr. Ar |
|---|---|---|---|---|---|---|---|
| 1 | 542 | 70.146 | 5.366 | 574.79 | 524.64 | 6.358 | 0.699 |
| 2 | 661.58 | 78.633 | 9.35 | 684.73 | 640.37 | 3.427 | 0.976 |
| 3 | 752.24 | 53.021 | 36.613 | 802.39 | 715.59 | 13.2 | 9.235 |
| 4 | 893.04 | 58.481 | 24.134 | 945.12 | 858.32 | 12.799 | 5.874 |
| 5 | 1157.29 | 47.478 | 18.93 | 1188.15 | 1114.86 | 16.87 | 4.116 |
| 6 | 1251.8 | 11.894 | 58.278 | 1303.88 | 1188.15 | 50.705 | 32.052 |
| 7 | 1327.03 | 58.25 | 19.729 | 1357.89 | 1303.88 | 8.908 | 3.142 |
| 8 | 1440.83 | 26.497 | 38.452 | 1475.54 | 1357.89 | 35.738 | 16.397 |
| 9 | 1575.84 | 23.472 | 39.914 | 1612.49 | 1537.27 | 28.117 | 12.792 |
| 10 | 1651.07 | 12.32 | 53.675 | 1732.08 | 1612.49 | 41.572 | 23.586 |
| 11 | 2565.33 | 48.47 | 5.1 | 2600.04 | 2509.39 | 25.986 | 1.707 |
| 12 | 2640.55 | 47.107 | 4.972 | 2684.91 | 2600.04 | 25.793 | 1.744 |
| 13 | 2860.43 | 36.696 | 3.052 | 2887.44 | 2760.14 | 46.822 | 1.576 |
| 14 | 3014.74 | 39.426 | 2.251 | 3253.91 | 2993.52 | 64.6 | 1.983 |
| 15 | 3309.85 | 41.042 | 17.009 | 3383.14 | 3253.91 | 37.539 | 7.278 |

**Fig. 2. IR Sample (S1) mefenamic acid**



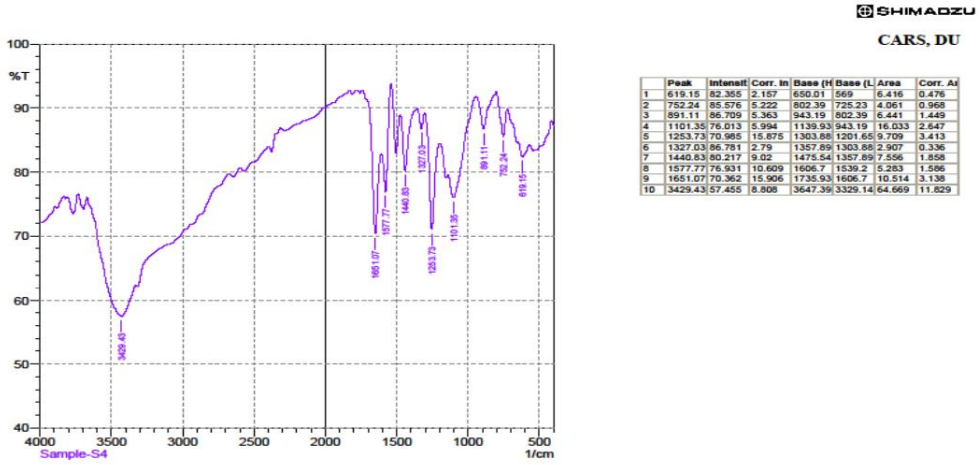

| | Peak | Intensit | Corr. In | Base (H | Base (L | Area | Corr. Ar |
|---|---|---|---|---|---|---|---|
| 1 | 480.28 | 86.027 | 2.96 | 540.07 | 414.7 | 7.392 | 1.073 |
| 2 | 599.86 | 82.136 | 3.823 | 632.65 | 540.07 | 6.618 | 0.699 |
| 3 | 657.73 | 79.416 | 7.59 | 692.44 | 632.65 | 4.532 | 1.018 |
| 4 | 997.2 | 81.846 | 11.649 | 1024.2 | 968.27 | 3.094 | 1.465 |
| 5 | 1097.5 | 78.113 | 5.341 | 1122.57 | 1024.2 | 7.706 | 1.429 |
| 6 | 1157.29 | 67.142 | 11.777 | 1182.36 | 1122.57 | 8.004 | 1.913 |
| 7 | 1201.65 | 73.968 | 5.542 | 1355.96 | 1182.36 | 10.659 | -1.977 |
| 8 | 1627.92 | 79.516 | 12.079 | 1743.65 | 1533.41 | 13.069 | 4.95 |
| 9 | 3444.87 | 41.827 | 26.362 | 3672.47 | 2401.38 | 248.184 | 78.446 |

**Fig. 3. IR Sample (S2) copper sulphate**



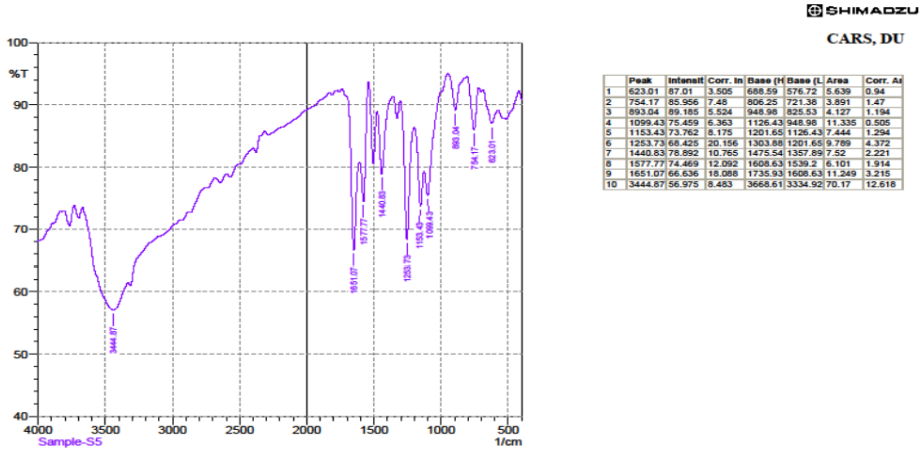

| | Peak | Intensit | Corr. In | Base (H | Base (L | Area | Corr. Ar |
|---|---|---|---|---|---|---|---|
| 1 | 626.87 | 75.781 | 10.04 | 692.44 | 586.36 | 8.686 | 2.031 |
| 2 | 740.67 | 87.679 | 3.783 | 854.47 | 692.44 | 6.974 | 1.441 |
| 3 | 1101.35 | 59.446 | 11.101 | 1128.36 | 997.2 | 17.7 | 3.441 |
| 4 | 1145.72 | 62.94 | 3.551 | 1338.6 | 1128.36 | 20.477 | -4.84 |
| 5 | 1618.28 | 63.843 | 22.063 | 1697.36 | 1502.55 | 19.824 | 7.549 |
| 6 | 3564.45 | 28.993 | 1.41 | 3680.18 | 3554.81 | 54.97 | 1.357 |

**Fig. 4. IR Sample (S3) zinc sulphate**



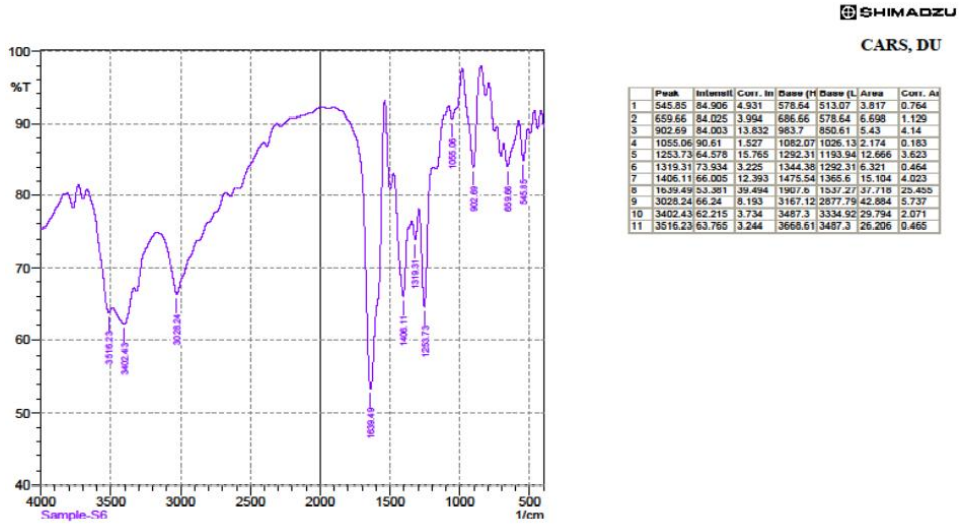

| | Peak | Intensit | Corr. In | Base (H | Base (L | Area | Corr. Ar |
|---|---|---|---|---|---|---|---|
| 1 | 619.15 | 82.355 | 2.157 | 650.01 | 569 | 6.416 | 0.476 |
| 2 | 752.24 | 85.576 | 5.222 | 802.39 | 725.23 | 4.061 | 0.968 |
| 3 | 891.11 | 86.709 | 5.363 | 943.19 | 802.39 | 6.441 | 1.449 |
| 4 | 1101.35 | 76.013 | 5.994 | 1139.93 | 943.19 | 16.033 | 2.647 |
| 5 | 1253.73 | 70.985 | 15.875 | 1303.88 | 1201.65 | 9.709 | 3.413 |
| 6 | 1327.03 | 86.781 | 2.79 | 1357.89 | 1303.88 | 2.907 | 0.336 |
| 7 | 1440.83 | 80.217 | 9.02 | 1475.54 | 1357.89 | 7.556 | 1.858 |
| 8 | 1577.77 | 76.931 | 10.609 | 1606.7 | 1539.2 | 5.283 | 1.586 |
| 9 | 1651.07 | 70.362 | 15.906 | 1735.93 | 1606.7 | 10.514 | 3.138 |
| 10 | 3429.43 | 57.455 | 8.868 | 3647.39 | 3329.14 | 64.669 | 11.829 |

**Fig. 5. IR Sample (S4) mixture of mefenamic acid & copper sulphate**




| | Peak | Intensit | Corr. In | Base (H | Base (L | Area | Corr. Ar |
|---|---|---|---|---|---|---|---|
| 1 | 623.01 | 87.01 | 3.505 | 688.59 | 576.72 | 5.639 | 0.94 |
| 2 | 754.17 | 85.956 | 7.48 | 806.25 | 721.38 | 3.891 | 1.47 |
| 3 | 893.04 | 89.185 | 5.524 | 948.98 | 825.53 | 4.127 | 1.194 |
| 4 | 1099.43 | 75.459 | 6.363 | 1126.43 | 948.98 | 11.335 | 0.505 |
| 5 | 1153.43 | 73.762 | 8.175 | 1201.65 | 1126.43 | 7.444 | 1.294 |
| 6 | 1253.73 | 68.425 | 20.156 | 1303.88 | 1201.65 | 9.789 | 4.372 |
| 7 | 1440.83 | 78.892 | 10.765 | 1475.54 | 1357.89 | 7.52 | 2.221 |
| 8 | 1577.77 | 74.469 | 12.092 | 1608.63 | 1539.2 | 6.101 | 1.914 |
| 9 | 1651.07 | 66.636 | 18.088 | 1735.93 | 1608.63 | 11.249 | 3.215 |
| 10 | 3444.87 | 56.975 | 8.483 | 3668.61 | 3334.92 | 70.17 | 12.618 |

**Fig. 6. IR Sample (S5) mixture of mefenamic acid & zinc sulphate**




| | Peak | Intensit | Corr. In | Base (H | Base (L | Area | Corr. Ar |
|---|---|---|---|---|---|---|---|
| 1 | 545.85 | 84.906 | 4.931 | 578.64 | 513.07 | 3.817 | 0.764 |
| 2 | 659.66 | 84.025 | 3.994 | 686.66 | 578.64 | 6.698 | 1.129 |
| 3 | 902.69 | 84.003 | 13.832 | 983.7 | 850.61 | 5.43 | 4.14 |
| 4 | 1055.06 | 90.61 | 1.527 | 1082.07 | 1026.13 | 2.174 | 0.183 |
| 5 | 1253.73 | 64.578 | 15.765 | 1292.31 | 1193.94 | 12.666 | 3.623 |
| 6 | 1319.31 | 73.934 | 3.225 | 1344.38 | 1292.31 | 6.321 | 0.464 |
| 7 | 1406.11 | 66.005 | 12.393 | 1475.54 | 1365.6 | 15.104 | 4.023 |
| 8 | 1639.49 | 53.381 | 39.494 | 1907.6 | 1537.27 | 37.718 | 25.455 |
| 9 | 3028.24 | 66.24 | 8.193 | 3167.12 | 2877.79 | 42.884 | 5.737 |
| 10 | 3402.43 | 62.215 | 3.734 | 3487.3 | 3334.92 | 29.794 | 2.071 |
| 11 | 3516.23 | 63.765 | 3.244 | 3668.61 | 3487.3 | 26.206 | 0.465 |

**Fig. 7. IR Sample (S6) mixture of EDTA & mefenamic acid**

### 3.2 Combination Data Analysis of Selective Compounds

Overall interpretation between mefenamic acid and selective metals were shown in (Fig. 08-10) and (Tables 1-3). Microsoft Excel (MS Excel, 2010) was used to analyze all data.

Here measured, any interaction between the drugs is an identical change to the IR pattern. Here mefenamic acid revealed its spectra of 3309 $cm^{-1}$, 3014 $cm^{-1}$, 2860 $cm^{-1}$, 1157 $cm^{-1}$ and 1575 $cm^{-1}$ indicating N-H, O-H, C-H & C=C groups. Copper metal was given spectra at 3444 $cm^{-1}$ & 1097 $cm^{-1}$. Besides mixture of mefenamic acid and copper metal revealed one spectrum for 3429 $cm^{-1}$ wavelength which has given no possible interaction because of the same wavelength. On the other hand, stretching peaks at 1327 $cm^{-1}$, 1651 $cm^{-1}$ & 1577 $cm^{-1}$ wavelength and the combination gets effective changes that alter the whole result of the FT-IR pattern. So there is a possible interaction with C=O, C-N & C=C groups formed respectively by $sp^3$, sp, and $sp^2$ hybridization [18].

**Table 1. IR interpretation of mefenamic acid, copper metal, and mixture, wavelength unit- cm-1**

| Interpretation | Wavelength Mefenamic acid ($cm^{-1}$) | Copper metal ($cm^{-1}$) | Mixture ($cm^{-1}$) |
|---|---|---|---|
| N-H | 3309 | N/A | N/A |
| O-H | 3014.74 | 3444.87 | 3429.43 |
| C-H | 2860.43 | N/A | N/A |
| C=O | 1157.29 | N/A | 1327.09 |
| C-N | N/A | N/A | 1651.07 |
| C=C | 1575.84 | N/A | 1577.77 |
| S=O | N/A | 1097.5 | 1101.35 |

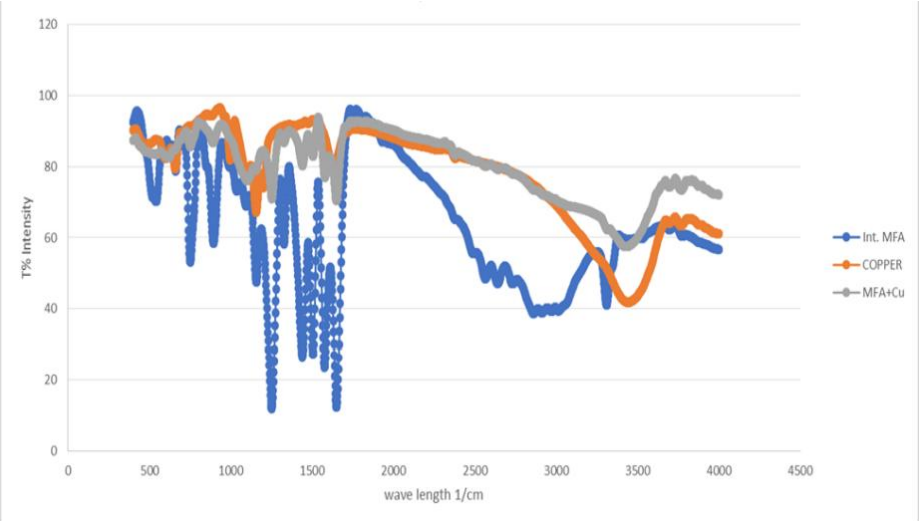



**Fig. 8. Combination of mefenamic acid, copper & mixture**

**Table 2. IR interpretation of mefenamic acid, zinc metal & mixture, wavelength unit-cm-1**

| Interpretation | Wavelength Mefenamic acid ($cm^{-1}$) | Zinc metal ($cm^{-1}$) | Mixture ($cm^{-1}$) |
|---|---|---|---|
| N-H | 3309 | N/A | 3444.87 |
| O-H | 3014.74 | 3564.45 | N/A |
| C-H | 2860.43 | N/A | N/A |
| C=O | 1157.29 | N/A | 1651 |
| C-N | N/A | N/A | N/A |
| C=C | 1575.84 | N/A | 1577.77 |
| S=O | N/A | 1101.35 | 1099.43 |

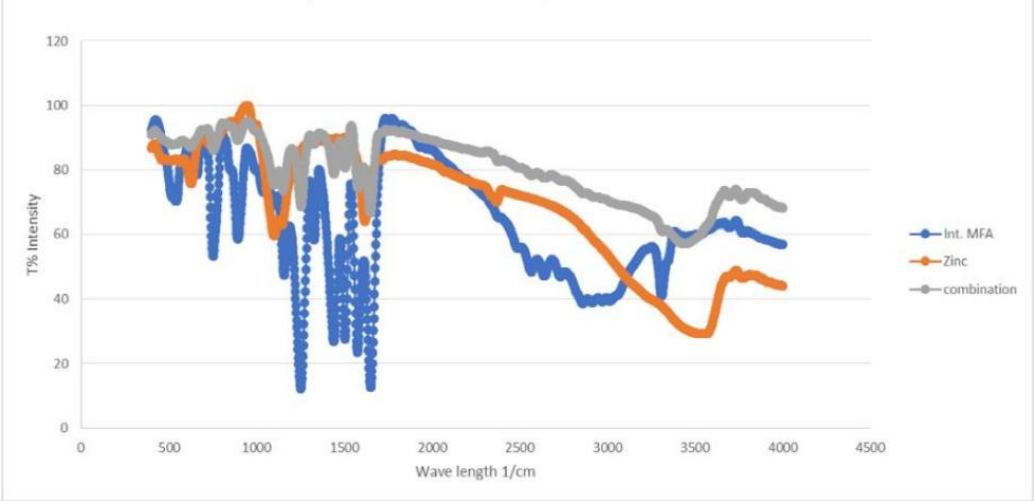



**Fig. 9. Combination of mefenamic acid, zinc & mixture**

**Table 3. IR interpretation of mefenamic acid, EDTA & mixture, wavelength unit- cm-1**

| Interpretation | Wavelength Mefenamic acid ($cm^{-1}$) | EDTA ($cm^{-1}$) | Mixture ($cm^{-1}$) |
|---|---|---|---|
| N-H | 3309 | N/A | 3402.43 |
| O-H | 3014.74 | 3776, 3431 | 3028.43 |
| C-H | 2860.43 | 2926 | N/A |
| C=O | 1157.29 | 1593 | 1406 |
| C-N | N/A | 1169 | 1319.31 |
| C=C | 1575.84 | 1029 | 1253.73 |
| S=O | N/A | 1080 | 1055.06 |

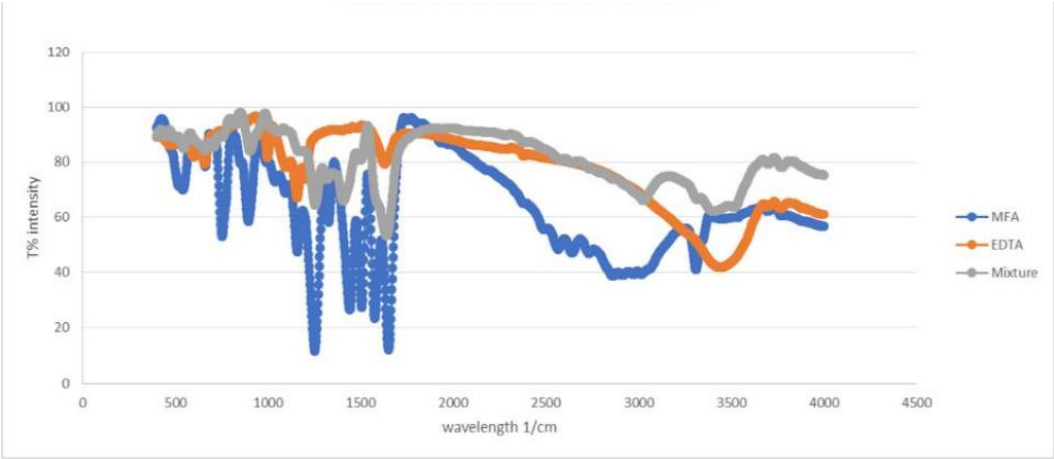



**Fig. 10. Combination of mefenamic acid, EDTA & mixture**

Here measured any interaction between the drugs is an identical change to the IR pattern. Here mefenamic acid revealed its spectra of 3309 $cm^{-1}$, 3014 $cm^{-1}$ , 2860 $cm^{-1}$ , 1157 $cm^{-1}$ & 1575 $cm^{-1}$ indicating N-H, O-H, C-H & C=C groups. Zinc metal was given spectra at 3444 $cm^{-1}$ & 1101 $cm^{-1}$. Besides mixture of mefenamic acid and copper metal revealed no spectra for wavelength, which have given no possible interaction because of the same wavelength. On the other hand, stretching peaks at 3444 $cm^{-1}$, 1651 $cm^{-1}$ & 1577 $cm^{-1}$ wavelength, and the

combination gets effective changes that alter the whole result of the FT-IR pattern. So there is a possible interaction with N-H, C-N & C=C groups formed respectively by $sp^3$, sp, and $sp^2$ hybridization [18].

Here measured, any interaction between the drugs is an identical change to the IR pattern. Here mefenamic acid revealed its spectra of 3309 $cm^{-1}$, 3014 $cm^{-1}$, 2860 $cm^{-1}$, 1157 $cm^{-1}$ and 1575 $cm^{-1}$ indicating N-H, O-H, C-H & C=C groups. EDTA was given spectra at (3776, 3431) $cm^{-1}$, 2926 $cm^{-1}$, 1593 $cm^{-1}$, 1169 $cm^{-1}$, 1029 $cm^{-1}$ & 1080 $cm^{-1}$. Besides mixture of mefenamic acid and EDTA revealed one spectrum for 3028 $cm^{-1}$, 1406 $cm^{-1}$ & 1253 $cm^{-1}$ wavelength, which have given no possible interaction because of the same wavelength. On the other hand, stretching peaks at 3402 $cm^{-1}$ wavelength, and the combination gets effective changes that alter the whole result of the FT-IR pattern. So there is a possible interaction with N-H groups formed respectively by $sp^3$ hybridization [18].

## 4. CONCLUSION

To reduce drug interactions, much research is being done to find novel medications. It is recently found that metal-based complexes decrease antiviral, antibacterial, and anticancer action. In order to construct actively functioning medications, it is vital to study the ability of physiologically active metal ions to interact with metalloproteinases like albumin, which transport and distribute these metal ions. The current research used the FT-IR spectroscopy technique to analyze interactions of $Cu^{2+}$, $Zn^{2+}$, and $EDTA^{4-}$ with mefenamic acid. Variations in the amino group of mefenamic acid after metal complexation demonstrated the metal ions' binding interactions. Metal ion interactions with acid products altered the functional structure, resulting in a negligible reduction in the mefenamic acid structure. All significant interactions were supported by the functional group of metal ions and drug product binding intensity. The present findings set a standard for repeatable mefenamic acid metal ion research.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## ACKNOWLEDGEMENTS

The authors would like to express their appreciation to the CARS (Centre for Advanced Research in Sciences) in University of Dhaka and the Laboratory of Pharmaceutical Technology & Cosmetology, Stamford University Bangladesh for their support, resources and infrastructural facilities required to conduct this research.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Topacli A, Ide S. Molecular structures of metal complexes with mefenamic acid. J Pharm Biomed Anal. 1999 [online];21(5):975-82.
   DOI: 10.1016/s0731-7085(99)00198-3, PMID 10703965.
2. Kovala-Demertzi D, Hadjipavlou-Litina D, Staninska M, Primikiri A, Kotoglou C, Demertzis MA. Anti-oxidant, in vitro, in vivo anti-inflammatory activity and antiproliferative activity of mefenamic acid and its metal complexes with manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II). J Enzyme Inhib Med Chem. 2009;24(3):742-52.
   DOI: 10.1080/14756360802361589, PMID 18720191.
3. Valentovic M. 'Mefenamic acid,' xPharm Compr. Pharmacol Ref. 2007:1-5.
   DOI: 10.1016/B978-008055232-3.62117-8.
4. Mavrikakis ME, Madkour MM, Buchanan WW. The place of mefenamic acid in the treatment of rheumatoid arthritis. Scott Med J. 1978;23(2):189-90.
   DOI: 10.1177/003693307802300223, PMID 306128.
5. Kowalczyk-Bronisz SH, Gieldanowski J. Activity of nonsteroid anti-inflammatory drugs in immunologically specific and nonspecific cellular responses. Arch Immunol Ther Exp (Warsz). 1976 [online];24(1):149-57.
   PMID 1083222.
6. Zucker MB, Peterson J. Effect of acetylsalicylic acid, other nonsteroidal anti-inflammatory agents, and dipyridamole on

human blood platelets. J Lab Clin Med. Jul 1970;76(1):66-75.

DOI: 10.5555/uri:pii:0022214370900958, PMID 5425364.

7. Khansari PS, Halliwell RF. Evidence for neuroprotection by the fenamate NSAID, mefenamic acid. Neurochem Int. 2009; 55(7):683-8.

DOI: 10.1016/j.neuint.2009.06.014,

PMID 19563851.

8. Halliwell RF, Thomas P, Patten D, James CH, Martinez-Torres A, Miledi R, et al. Subunit-selective modulation of GABAA receptors by the nonsteroidal anti-inflammatory agent, mefenamic acid. Eur J Neurosci. 1999;11(8):2897-905.

DOI: 10.1046/j.1460-9568.1999.00709.x

PMID 10457186.

9. Tall AR, Mistilis SP. Studies on Ponstan (mefenamic acid): I. Gastrointestinal blood loss; II. Absorption and excretion of a new formulation. J Int Med Res. 1975;3(3):176-82.

DOI: 10.1177/030006057500300306

PMID 162673.

10. Hébert JG, Le Morvan P, Bourgouin J. Double-blind comparison of ketoprofen and mefenamic acid in the treatment of primary dysmenorrhea. Clin Ther. 1986 [online];8(3):329-35.

PMID 3521860.

11. Serfaty D. A Comparative Crossover Study of piroxicam vs. mefenamic acid and diclofenac in France. Acta Obstet Gynecol Scand Suppl. 1986;138(S138):19-20.

DOI: 10.3109/00016348509157062

PMID 3548207.

12. Anderson AM, Fraser IS, Haynes PJ, Turnbull AC. Trial of prostaglandin-synthetase inhibitors in primary DYSMENORRHŒA. Lancet. Feb 1978; 311(8060):345-8.

DOI: 10.1016/S0140-6736(78)91077-2

13. Barnard-Jones K, Davies RW, Lalla O, Mann PG, Welch RB. Mefenamic acid versus ibuprofen in osteoarthritis--a double-blind cross-over study. Br J Clin Pract. Dec 1986 [online];40(12):528-31.

PMID 3307863.

14. Buchmann E. Mefenamic acid compared with indomethacin and placebo in osteoarthritis. Rheumatology. 1966;VIII, no. suppl_1:119-25.

DOI:10.1093/rheumatology/VIII.suppl_1.119

15. Al-Waili NS. Treatment of menstrual migraine with prostaglandin synthesis inhibitor mefenamic acid: double-blind study with placebo. Eur J Med Res. 2000 [online];5(4):176-82.

PMID 10799353.

16. Weiss CF, Harris ST, Barrow WB, Buchanan RA. Mefenamic acid— An antipyretic for use in children. J Pediatr. Jun 1968;72(6):867-70.

DOI: 10.1016/S0022-3476(68)80444-5

PMID 5652617.

17. Cimolai N. The potential and promise of mefenamic acid. Expert Rev Clin Pharmacol. 2013;6(3):289-305.

DOI: 10.1586/ecp.13.15

PMID 23656341.

18. Zapała L, Kosińska M, Woźnicka E, Byczyński Ł, Zapała W. Synthesis, spectral and thermal study of La(III), Nd(III), Sm(III), Eu(III), GD(III) and Tb(III) complexes with mefenamic acid. J Therm Anal Calorim. Apr 2016;124(1):363-74.

DOI: 10.1007/s10973-015-5120-0

19. Etcheverry SB, Barrio DA, Cortizo AM, Williams PAM. Three new vanadyl (IV) complexes with nonsteroidal anti-inflammatory drugs (ibuprofen, naproxen and tolmetin). Bioactivity on osteoblast-like cells in culture. J Inorg Biochem. 2002; 88(1):94-100.

DOI: 10.1016/s0162-0134(01)00368-3

PMID 11750030.

20. Feng J, Du X, Liu H, Sui X, Zhang C, Tang Y, et al. Manganese-mefenamic acid complexes exhibit high lipoxygenase inhibitory activity. Dalton Trans Dalt, translator. 2014;43(28):10930-9.

DOI: 10.1039/c4dt01111b

PMID 24903101.

21. Ashraf A, Siddiqui WA, Akbar J, Mustafa G, Krautscheid H, Ullah N, et al. Metal complexes of benzimidazole derived sulfonamide: synthesis, molecular structures and antimicrobial activity. Inorg Chim Acta. 2016;443:179-85.

DOI: 10.1016/j.ica.2015.12.031

22. Sharma RP, Singh S, Singh A, Ferretti V. Spectra-structure relationship: Synthesis, characterization of copper(II) complexes with ibuprofenate, o-methoxybenzoate, p-ethoxybenzoate and single crystal X-ray structure determination of [trans-Cu(en)2(H2O)2](L)2 where en = ethylenediammine, L = o-met. J Mol Struct. 2009;918(1-3):188-93.

DOI: 10.1016/j.molstruc.2008.08.003



*Peer-review history:*
*The peer review history for this paper can be accessed here:*
*https://www.sdiarticle5.com/review-history/97044*