

# Mechanochemical Preparation and Biological Activity of Mn (II) Complex from Ciprofloxacin

Shehu Jibril<sup>1,\*</sup>, Kabiru Aliyu Baraya<sup>1</sup>, Auwal Adamu Mahmoud<sup>2</sup>, Jibril Shirama<sup>1</sup>, Samira Muhammad Shehu<sup>1</sup>, Shu'aibu Bala Adamu<sup>3</sup>

<sup>1</sup>Department of Chemistry, Aminu Saleh College of Education, Azare, Nigeria

<sup>2</sup>Department of Chemistry, Abubakar Tafawa Balewa University, Bauchi, Nigeria

<sup>3</sup>Department of Biology, Aminu Saleh College of Education, Azare, Nigeria

## Email address:

shehuusmanjibril@yahoo.com (S. Jibril)

\*Corresponding author

## To cite this article:

Shehu Jibril, Kabiru Aliyu Baraya, Auwal Adamu Mahmoud, Jibril Shirama, Samira Muhammad Shehu, Shu'aibu Bala Adamu.

Mechanochemical Preparation and Biological Activity of Mn (II) Complex from Ciprofloxacin. *World Journal of Applied Chemistry*.

Vol. 7, No. 1, 2022, pp. 24-28. doi: 10.11648/j.wjac.20220701.14

Received: February 8, 2022; Accepted: March 7, 2022; Published: March 18, 2022

**Abstract:** The mechanochemically prepared complex  $[Mn(cip)_2Cl_2]$  was synthesized using simple neat grinding method and analyzed using spectral studies, elemental analysis and physicochemical properties. The complex shows increase in biological activity compared with both the free ligand of ciprofloxacin and the standard. The IR spectral analysis of the complex, the ligand ciprofloxacin acts as bidentate ligand that indicate a strong band in the spectra at  $1707.92\text{ cm}^{-1}$  and  $1628.81\text{ cm}^{-1}$  which was assigned to  $\nu(C=O)\text{ cm}^{-1}$   $\nu(COO)\text{ cm}^{-1}$ . It shifted to a lower frequency's regions of  $1707.92\text{ cm}^{-1}$  and  $1625.40\text{ cm}^{-1}$  in the complex indicating the involvement of carbonyl groups of both amide and carboxylic acid in the coordination, the bands at  $478.20\text{ cm}^{-1}$  and  $750.39\text{ cm}^{-1}$  which is absent in the free ligand appeared in the complex was assigned to  $\nu(M-O)$  and  $\nu(M-Cl)$  band. The value obtained from molar conductivity at  $10.7\text{ }\Omega^{-1}\text{cm}^2\text{mol}^{-1}$  indicate that the complex is non-electrolyte in DMSO. Both the elemental and physicochemical analysis agreed with the proposed structure of the compound and also suggested one metal to two ligands ratio. Due to environmentally friendly, shortest reactions time, inexpensive, production of higher yields the authors recommend the use of mechanochemical methods over solution-based.

**Keywords:** Mechanochemically, Prepared, Complex, Ciprofloxacin

## 1. Introduction

As formalized by IUPAC, a mechanical-assisted reaction is "a reaction caused by the mechanical energy". In fact, mechanical actions, such as compression, stress, or friction, usually provides the energy to activate a process. The principal feature of mechanical-assisted process is the achievement of chemical changes by the only action of grinding (or milling), without needing to dissolve reagents (therefore without using any solvent) [1]. Grinding is a broad term that describes the effect of mechanical forces on a compound that allows a solid breaking into small parts. By grinding, the improved potential energy together with friction and shear contributions, generate surface and shape defects in the reactants.

This enabling technology is characterized by mechanical grinding of reactants and induces chemical reactivity by mechanical force (e. g. by compression, shear, or friction) [2]. In general, mechanochemical provides advantages such as prevent the use of excessive solvent, short reaction time, high efficiency, well as being more cost effective than traditional synthesis [3]. Nowadays, A firmly established application of modern mechanochemistry is generally in medicinal chemistry which termed as "medicinal mechanochemistry". Several researchers reported the mechanochemical synthesis of drugs, for example [4] reported the liquid-assisted mechanochemistry in the synthesis of pharmaceuticals. To date, mechanochemical approaches being applied to

transformations from across the chemical sciences have been reported, spanning from the synthesis of inorganic and organic compounds.

This research work aims to mechano-chemically prepared Mn (II) complex of ciprofloxacin and also to determine how metal-drug binding influence the activity of the drug.

## 2. Materials and Methods

### 2.1. Materials

The reagents used were of analytical grade and used without any further purification. The API of Ciprofloxacin was obtained from Bristol Scientific-Sigma Aldrich. Metal salt used is  $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ . Glass wares used in the work were washed thoroughly, rinsed with distilled water and dried in an oven at  $110^\circ\text{C}$ . Weighing balance of model B154 Mettler Toledo was used during the experiment. Stuart melting point apparatus SMP0 was used to determine the melting point, Jenway conductivity meter model 4010 ( $10^{-3}\text{g}$  in 10ml DMSO) was used in determining molar conductance, while magnetic moment of the complexes was obtained using Magnetic susceptibility balance of Sherwood scientific Cambridge UK. Elemental analysis was carried out using Series II CHNS/O Analyzer 2400 and metal content of the complexes was determined in AA240FS, Fast Sequential Atomic Absorption Spectrometer. The FTIR spectra were recorded as KBr on FTIR-8400S in the range of  $4000\text{--}400\text{cm}^{-1}$  while the electronic spectra of the complexes were recorded using ultraviolet spectrometer lambda 35 with the range of  $200\text{--}700\text{nm}$ . The biological activity was determined using agar-well diffusion method.

### 2.2. Mechanochemical Preparation of the Complex

The method [5] was modified and adopted for the preparation of the complex by simple grinding of 2 mmol (0.66g) of ciprofloxacin with 1 mmol (0.166g) of  $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$  in a mortar and pestle for about 10 minutes until a clear yellow powder was obtained as a product. The product obtained were dried in desiccator.

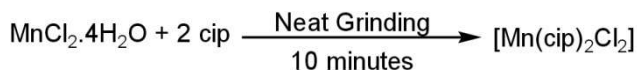


Figure 1. Formation of  $[\text{Mn}(\text{cip})_2\text{Cl}_2]$ .

### 2.3. Antibacterial Screening

The [6] method was used in which 0.02 g of both metal (II) complex and the ligand were each dissolved in 1 ml of Dimethyl sulfoxide (DMSO) to gives a stock solution using half serial doubling dilution method of  $20 \mu\text{g/ml}$ ,  $10 \mu\text{g/ml}$  and  $5 \mu\text{g/ml}$  which were placed on the surface of the culture media and incubated at room temperature for 48hrs. Then *in vitro* antibacterial activity against *Escherichia coli*, *Salmonella Typhi* and *Staphylococcus aureus* were carried out by agar-well diffusion method. Standard was used to compare with the diameter of zone of inhibition produced by ligands and complexes.

## 3. Results and Discussion

The prepared complex was completed within shorter period of 10 minutes to yield a higher yield and yellow colour compound with a melting point of  $300^\circ\text{C}$  which is higher than the free ligand of ciprofloxacin due to coordination with the metal ion as presented in Table 1 [7].

Table 1. The Physical Properties of Ciprofloxacin and its Metal (II) Complex.

Compounds	Colour	Melting point ( $^\circ\text{C}$ )	D/ temperature ( $^\circ\text{C}$ )	Molar Conductivity ( $\Omega^{-1}\text{cm}^2\text{mol}^{-1}$ )	Effective magnetic moment (BM)
Ciprofloxacin	White	255	-	-	-
$[\text{Mn}(\text{Cip})_2\text{Cl}_2]$	Yellow	-	300	10.07	5.5

The conductivity as presented in Table 1 was measured in DMSO ( $10.07 \Omega^{-1}\text{cm}^2\text{mol}^{-1}$ ) which fall within the range of non-electrolytes in DMSO [8] which was frequently used to elucidate the geometry of the complex.

The suggestion of the likely geometry of complexes can also be

provided by their magnetic moment. The magnetic moment of 5.5BM as in Table 1 is tentatively proposed high spin octahedral geometry since the value lies within the range that correspond to spin-only value magnetic moment for high spin octahedral geometry around Mn (II) ion as reported in the literature [9].

Table 2. The elemental analysis data of the complex.

Compounds	Molecular formula (Molar Mass)	Elemental analysis: found (calculated)%			
		C	H	N	M
$[\text{Mn}(\text{Cip})_2\text{Cl}_2]$	$\text{C}_{17}\text{H}_{18}\text{FN}_3\text{Cl}_2\text{Mn}$ (789)	25.99 (25.86)	2.80 (2.28)	4.00 (5.32)	15.29 (15.97)

### 3.1. Elemental Analysis

The elemental analysis data obtained are presented in Table 2 in which both the percentage of C, H, N and Metal ion proved the proposed structure of the complex  $[\text{Mn}(\text{cip})_2\text{Cl}_2]$  [10].

### 3.2. Infrared Spectra

The infrared spectra for both the free ligand of ciprofloxacin (Cip) and metal complex are given in Figure 2 and Figure 3 respectively, while the IR data are presented in Table 3 and compared [11].

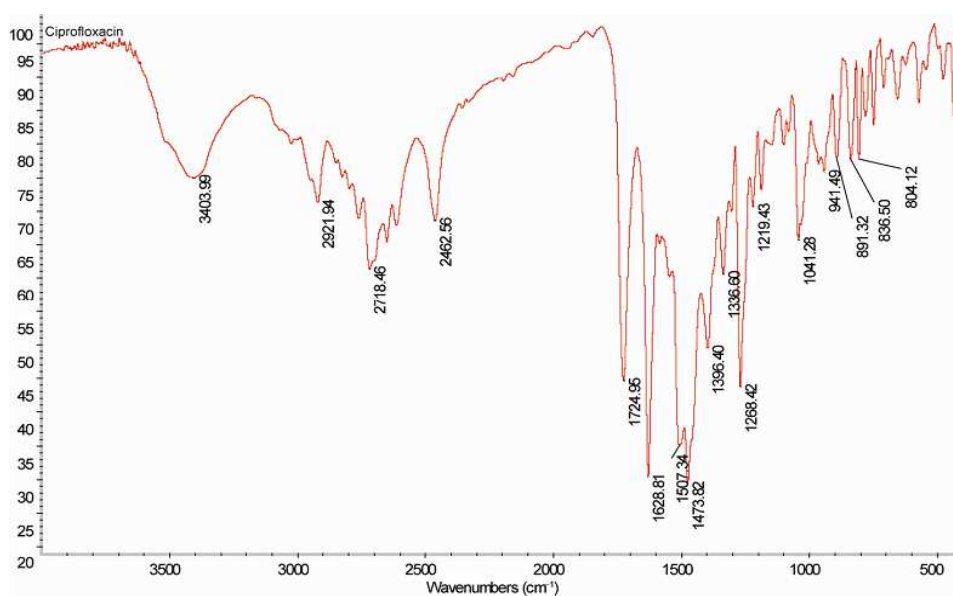
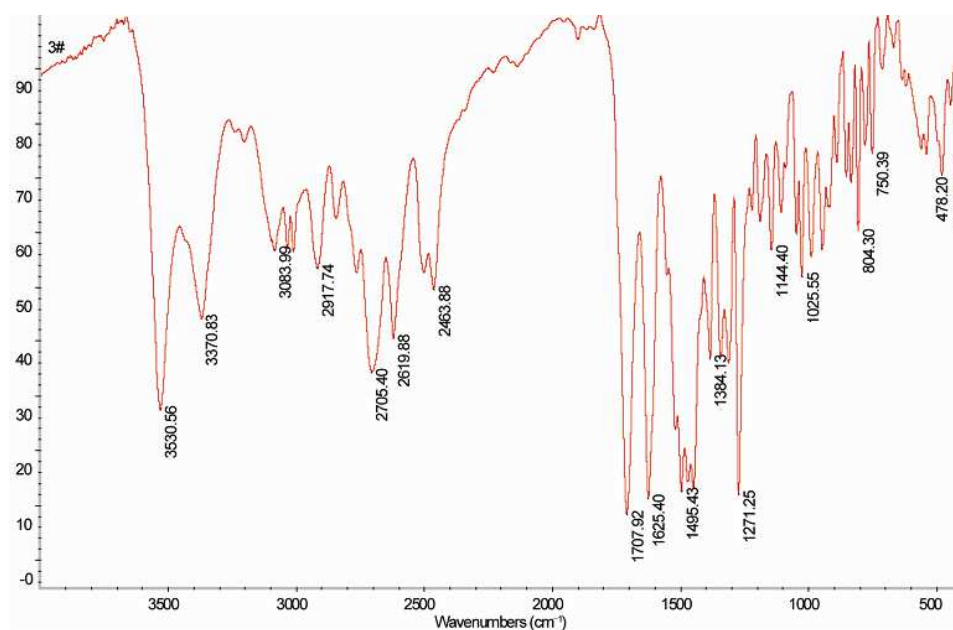
**Table 3.** The IR Spectra Data of Ciprofloxacin and its Metal (II) complex.

Compound	$\nu(\text{O-H}) \text{ cm}^{-1}$	$\nu(\text{COO}) \text{ cm}^{-1}$	$\nu(\text{C=O}) \text{ cm}^{-1}$	$\nu(\text{C-O}) \text{ cm}^{-1}$	M-O	M-Cl
Ciprofloxacin	3403.99	1628.81	1724.95	1473.82	-	-
[Mn(Cip) <sub>2</sub> Cl <sub>2</sub> ]	3530.56	1625.40	1707.92	1495.43	478.20	750.39

Keys:  $\nu$ =Wave number, M= Metal, O= Oxygen, Cl=Chlorine.

**Table 4.** Electronic spectra in DMSO solvent for the ciprofloxacin and metal complex with the suggested geometry.

Compounds	Electronic Spectra			Suggested Geometry
	Wavelength (nm)	Energy ( $\text{cm}^{-1}$ )	Assignments	
Ciprofloxacin	205	48780	$n \rightarrow \pi^*$	-
	210	47619	$\pi \rightarrow \pi^*$	
[Mn(Cip) <sub>2</sub> Cl <sub>2</sub> ]	221	45248	${}^6\text{A}_{1g} \rightarrow {}^6\text{A}_{1g}$	Octahedral
	237	42194	MLCT	

**Figure 2.** Infrared Spectrum of Ciprofloxacin.**Figure 3.** Infrared Spectrum of Ciprofloxacin Manganese.

The infrared spectral of the ligand (ciprofloxacin) shows the bands at 1724.95  $\text{cm}^{-1}$  and 1628.81  $\text{cm}^{-1}$  which was both assigned to  $\nu(\text{C}=\text{O})$  and  $\nu(\text{COO})$  vibrational frequency and re-appeared at 1707.92  $\text{cm}^{-1}$  and 1625.40  $\text{cm}^{-1}$  in the complex which is difference in the free ligand as it provide evidence of coordination through both the carbonyl groups, as presented in the literature [12]. The new bands which are not present in the spectrum of the ligand at 478.20  $\text{cm}^{-1}$  and 750.39  $\text{cm}^{-1}$  is assigned to M-O and M-Cl vibration which support the involvement of O and Cl atoms in the complexation with metal ion under investigation. Similar results were reported by [13].

### 3.3. Electronic Spectra

Electronic spectra are presented in Table 4 in which the ligand ciprofloxacin shows two bands at 205nm and 210nm which were assigned to  $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$  [14], while in the complex the bands re-appeared at 221nm and 237nm is assigned to  ${}^6\text{A}_{1g} \rightarrow {}^6\text{A}_{1g}$  and MLCT transition. This transition is within typical of octahedral geometry around metal ion [14].

### 3.4. Biological Activity

Biological activity test is presented in table 5.

**Table 5.** Anti-bacterial Activity Test of Ciprofloxacin and its Metal (II) complex.

Compounds	Concentration ( $\mu\text{g}$ / agar-well)	Inhibition Zones		
		S. aureus (mm)	E. coli (mm)	S. typhi (mm)
Ciprofloxacin	5	13	15	18
	10	17	20	19
	20	24	25	22
[Mn(Cip) <sub>2</sub> Cl <sub>2</sub> ]	5	29	19	-
	10	32	26	19
	20	35	32	26
Standard (Gentamycin)	20	27	37	44

S. aureus = Staphylococcus aureus, E. coli = Escherichia coli, S. typhi=Salmonella typhi.

The complex is active against bacteria isolates in both higher concentration of 10 $\mu\text{g}$  and 20 $\mu\text{g}$  while inactive against 5 $\mu\text{g}$  *Salmonella Typhi*. Generally, the complex shows significant antibacterial strength and these values are compared with the standard of Gentamycin [15].

## 4. Conclusion

These results revealed that metal-drug complexes can be prepared mechanochemically. The spectral studies also revealed the coordination of the ligand to the metal ion through both the carbonyl groups in the ligand making the ligand to be bidentate and the complex to be octahedral geometry. Elemental analysis proved the proposed structure of the complex and biological activity of the complex shows increases compared with the ligand.

## 5. Recommendation

Of all solid-state techniques, mechanochemistry is becoming the focal point of efforts to design solid-state syntheses. Often found to lead to shorter reaction times and higher yields than its solution counterparts.

## Acknowledgements

The Authors acknowledge the support and contributions given to them from Tet fund through Aminu Saleh College of Education, Azare.

## References

- [1] Cova, C. M., & Luque, M. (2019). Advances in mechanochemical processes for biomass valorization. *BMC Chemical Engineering*, 1 (16), 1-12.
- [2] Takacs, L. (2013). The historical development of mechanochemistry. *Chemical Society Review*, 42, 7649–7659. DOI: 10.1039/c2cs35442j.
- [3] Cao, Q., Stark, R. T., Fallis, I. A., Browne, D. L. (2019). A ball-milling-enabled Reformatsky reaction. (Wiley Online Library). *ChemSusChem Communications*, 12, 2554–2557. doi: 10.1002/cssc.201900886.
- [4] Ying, P., Yu, J., & Su, W. (2021). Liquid-assisted grinding mechanochemistry in the synthesis of pharmaceuticals. *Advanced Synthesis and Catalysis*, 363, 1246– 1271. DOI: 10.1002/adsc.202001245.
- [5] Mottillo, C., & Frišcic, T. (2017). Advances in solid-state transformations of coordination bonds: from the ball mill to the aging chamber. *Molecules*, 22 (144), 1-38.
- [6] Yusha'u, M. (2011). Phytochemical screening and antibacterial activity of hibiscus sabdariffa extract against some urinary tract isolates. *Biological and Environmental Journal for the Tropics*, 8 (2), 83-86.
- [7] Mustapha, A. N., Ndahi, N. P., Paul B. B., & Fugu M. B. (2014). Synthesis, characterization and antimicrobial studies of metal (II) complexes of ciprofloxacin. *Journal of Chemical and Pharmaceutical Research*, 6 (4), 588-593.

- [8] Ali, I., Wani, W. A., & Saleem, K. (2013). Empirical formulae to structures of metal complexes by molar conductance. *Synthesis and Reactivity in Inorganic, Metal-Organic and Nano-Metal Chemistry*, 4 (43), 1162-1170.
- [9] Al-Noor, T. H., Al- Jeboori, A. T., & Aziz, M. M. (2013). Synthetic, spectroscopic and antibacterial studies of Fe (II), Co (II), Ni (II), Cu (II) and Zn (II) mixed ligand complexes of nicotinamide and cephalexin antibiotics. *Chemistry and Materials Research*, 3 (3), 114-125.
- [10] Waziri, I., Mala G. A., Fugu, M. B., Isah, B., & Umaru, U. (2017). Synthesis, spectral characterization and antimicrobial activity of some metal complexes of mixed antibiotics. *Chemistry Research Journal*. 2 (2) 52.
- [11] Bamigboye, M. O., & Ahmed, M. N. (2019). Chelation, physicochemical and antimicrobial activities of some mixed cloxacillin-vitamin C metal complexes. *Journal of Applied and Fundamental Sciences*, 5 (2), 66-73.
- [12] Kothari, R., & Agrawal, A. (2015). Synthesis, spectroscopic characterization and biological evaluation of ciprofloxacin macrocyclic copper (II) complexes. *World Journal of Pharmacy and Pharmaceutical Sciences*, 4 (06), 1062-1073.
- [13] Eugene-Osoikhia, T. T., Aleem, A. O., & Ayeni, F. (2020). Synthesis, characterization and antimicrobial studies of mixed ligands metal (II) complexes of sulfamethoxazole and N, N-donors' heterocycles. *FUDMA Journal of Sciences (FJS)*, 4 (2), 217 – 232.
- [14] Hashim, A. S., Ali, E. A., & Ahmed, K. (2015). Synthesis and characterization of Al (III) complex with paracetamol. *International Journal of Pharmaceutical Quality Assurance*, 10 (1), 156-159.
- [15] Sani, S., & Siraj, I. T. (2021). Copper (II) and Zinc (II) complexes synthesized by green mechanochemical method and their antimicrobial studies. *Communication in Physical Science*, 7 (2), 73-81.