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Mechanochemical Synthesis as a Panacea for Environmental Contamination

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Abstract

The researchers in this paper use mechanochemical synthesis as a panacea for the excess use of solution based syntheses that cause environmental contamination. The main aimed of the paper is the usage of mechanochemicaly synthesized complex of ciprofloxacin which was characterized by physical methods, spectral and biological studies. Spectral studies show that; in the complexe, the ciprofloxacin acted as bidentate ligand which coordinated to the metal ion through the ring carbonyl oxygen and one of the oxygen atoms of the carboxylate group. Results from microanalysis data shows 1:2 metal to ligand ratio. All the complexes show strong antibacterial activity at all concentrations compared with the free ligand (ciprofloxacin). Due to environmentally friendly, shortest reactions time, inexpensive, production of higher yields. Therefore, the authors recommend the use of mechanochemical methods over solution-based.

Keywords: *Mechanochemical, Synthesis, Ciprofloxacin, Panacea, Solution-based*

Introduction

According to Wilhelm Ostwald in (1835-1932) classified mechanochemistry as a branch of chemistry along with thermochemistry, electrochemistry, and photochemistry (James et al., 2012) in which mechanochemical actions normally induces chemical changes in different situations either intentionally or unintentionally (Takacs, 2007). Therefore, mechanochemical synthesis refers to the reactions in which solid reactants are induced by the input of mechanical energy by grinding using manual ball mills or manual methods (James et al., 2012). It is becoming more intensely studied partly because it can promote reactions between solids quickly and quantitatively, with either no added solvent or only nominal amounts. Historically it has been a sideline approach to chemical synthesis, and solution-based methods have been adopted by default. However, mechanochemistry could in future become a more mainstream technique for two reasons. Firstly, it is increasingly clear that is effective, and even advantageous, in ever-widening types of synthesis. Secondly, our current dependence on solvents appears increasingly unsustainable since it is wasteful of fossil-derived materials (e.g. 85% of chemicals used in the pharmaceutical industry are solvents and even if recycled typical recovery rates are only 50–80%), environmentally problematic, hazardous and energy-demanding with regard to solvent production, purification and recycling (Dubois et al., 2014).The needs for cleaner and hazardous free environment derived researchers into mechanochemical synthesis.

Statement of the Problem

As earlier stated, the research work looks at the alternative synthetic route to solution-based synthesis that cause environmental problematic. Therefore, the focus in this article is the use of mechanochemical transformation of metal (II) complex derived from ciprofloxacin by net grinding method and to compare the activity of the complex, ligand and standard against selected bacteria isolates. This means there is for the research.

Objective of the Study

The major objective of the study is to synthesized metal (II) complex of ciprofloxacin via mechanochemical means and their characterization in order to minimize the use of solvent that cause hazardous, environmental problematic and so forth.

Significance of the Study

The study designed to address the followings

i. The use of mechanochemical synthesis approach for the reliable synthesis of coordination metal (II) complexes of active pharmaceutical ingredient (API)
ii. To limit the use of solvent in chemical synthesis. Since it is wasteful of fossil-derived materials that cause hazardous and environmental problematic
iii. To give high product yield obtained mechanochemically, fast, low cost and eco-friendly.

Materials and Methods

Materials

All the reagents were of analytical grade and used without any further purification. The active pharmaceutical ingredient of Ciprofloxacin was obtained from Bristol Scientific-Sigma Aldrich. Metal salt used include $CoCl_2.6H_2O$. All the glass wares used in the work were washed thoroughly with detergent, rinsed with distilled water and dried in an oven at 110^oC. Weighing balance of model B154 Mettler Toledo was used throughout the experiment. The melting point of the complex was determined using Stuart melting point apparatus SMP0, molar conductance was obtained in Jenway conductivity meter model 4010 (10-3g in 10ml DMSO), while magnetic moment of the complex was obtained using Magnetic susceptibility balance of Sherwood scientific Cambridge UK. The elemental analysis was carried out using Flash 2000 Organic elemental analyzer 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 4000-400cm-1 while the electronic spectra of the complex was recorded using ultraviolet spectrometer lambda 35 with the range of 200-700nm. The antibacterial evaluation of the complex was determined using agar-well diffusion method.

Synthesis of the Complex

The described method by (Tella et al., 2011) was adopted and modified for the synthesis of the complex. 2 mmol (660mg) of Ciprofloxacin were mixed with 1 mmol (239mg) of $CoCl_2.6H_2O$ separately in mortar and pestle for about 10-15minutes in 2:1 ratio. The colour product obtained was dried in desiccator.

$$M + 2Cip \xrightarrow{\text{Neat Grinding}} [M(Cip)_2Cl_2]$$

Where M = $CoCl_2$

Antibacterial Screening

The described method by (Yusha'u, 2011) in which 0.02 g of ligand and metal (II) complex was dissolved in 1 ml of Dimethyl sulfoxide (DMSO) to gives a stock solution by half serial doubling dilution method of 20 µg/ml, 10 µg/ml and 5 µg/ml which were placed on the surface of the culture media and incubated at room temperature up to 2 days. Then in *vitro* antibacterial activity against *Escherichia coli, Salmonella Typhi* and *Staphylococcus aurous* were carried out by agar-well diffusion method. Standard was used to compare with the diameter of zone of inhibition produced by ligands and complex.

Results and Discussion

The reaction of the synthesized complex was completed within short period of time. The product yielded higher yield and gray colour complex of $[Co(Cip)_2Cl_2]$, similar to the results reported by (Mustapha et al., 2014) the complex is non-hygroscopic with melting point of 297 ^{0}C which is higher than the free ligand of 255 ^{0}C due to complexation (Mustapha et al., 2014). The physical properties of both the ligand and the complex are presented in Table 1. Co (II) complex is soluble in DMSO, soluble in non-polar and insoluble in polar solvents.

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

Compounds	Colour	Melting point (^{o}C)	D/ temperature (^{o}C)	Molar Conductivity ($\Omega^{-1}cm^2mol^{-1}$)	Effective magnetic moment (BM)
Ciprofloxacin	White	255		-	-
$[Co(Cip)_2Cl_2]$	Gray	-	297	10.43	5.7

Molar conductance can be used to elucidate the structure of the complexes as reported by Ali et al. (2013), the molar conductivity value presented in Table 1 rendered the complex to be non-electrolyte in DMSO solvent (Ali et al.,2013). Also, magnetic moment frequently has been used to suggest the likely geometry of the complex. The μeff value of 5.7BM as presented in Table 1 is tentatively proposed high spin octahedral geometry due to the presence of unpaired electrons around the metal ion. These value lie within the expected range for high spin octahedral geometry as reported in the literature of (Al-Noor et al., 2013).

Table 2: ***The microanalysis data of the complexes***

Compounds	Molecular formula (Molar Mass)	Microanalysis: found (calculated) %			
		C	H	N	M
[Co(Cip)$_2$Cl$_2$]	$C_{17}H_{18}FN_3Cl_2Co$ (793)	25.92 (27.73)	2.56 (2.27)	5.10 (5.30)	7.27 (7.44)

Microanalysis

The microanalysis results obtained for the complex are presented in Table 2. Both the % of C, H, N and metal ion agreed with the proposed structure due to the evaluation of the microanalysis data and also showed the compound as [CO(Cip)$_2$Cl$_2$] (Al-Noor et al., 2013).

Infrared Spectral Analysis

The IR spectra are presented in Table 3 by comparing of ligand spectra with metal complex as reported in the literature of (Waziri et al., 2017).

Table 3: ***The IR Spectra Data of Ciprofloxacin and its Metal (II) complexes***

Compound	υ(O-H) cm^{-1}	υ(COO) cm^{-1}	υ(C=O) cm^{-1}	υ(C-O) cm^{-1}	M-O	M-Cl
Ciprofloxacin	3403.99	1628.81	1724.95	1473.82	-	-
[Co(Cip)$_2$Cl$_2$]	3385.92	1580.29	1632.89	1521.09	509.89	707.38

Keys: υ=Wave number, M= Metal, O= Oxygen

Table 4: ***Electronic spectra in DMSO solvent for the ciprofloxacin and metal complexes with their suggested geometry***

Compounds	Electronic Spectra			Suggested Geometry
	Wavelength (nm)	Energy (cm^{-1})	Assignments	
Ciprofloxacin	205	48780	$n \rightarrow \pi^*$	
	210	47619	$\pi \rightarrow \pi^*$	
[Co(Cip)$_2$Cl$_2$]	215	46512	$^4T_{1g} \rightarrow {}^4T_{1g}$	Octahedral

245	40816	$^4T_{1g}\rightarrow^4T_{2g}$
251	39840	$^4T_{1g}\rightarrow^4A_{2g}$

The IR spectral data of both the ciprofloxacin and its metal (II) complex suggested that; the band at 1724.95cm^{-1} in the free ligand (Ciprofloxacin) is assigned to υ(C=O) and shifted to 1632.80cm^{-1} for the complex. Band at 1628.81cm^{-1} in the spectrum of ligand has been attributed to υ(COO) vibrational frequency, this band also, appeared to shifted in the spectra of the complexes as presented in Table 3 which suggests the coordination through O atom of the carboxylate group. These results obtained agreed with the literature of (Kothari & Agrawal, 2015). The υ(O-H) band at 3403.99cm^{-1} in the ligand also shifted to 3385.92cm^{-1} in the complex shows a new compound is formed (Refat et al., 2014). The bands at 509.89cm^{-1} and 707.38 cm^{-1} in the complex which could not be traced in the spectrum of free ligand is assigned to M-O and M-Cl band. Similar observation was made by Mustapha et al., 2014).

Electronic Spectral Analysis

Table 4 present the electronic spectra of both the free ligand (ciprofloxacin) and its metal (II) complex. The ligand shows two bands at 205nm and 210nm which could be assigned to n $\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ (Waziri et al., 2017). These absorption bands appeared into three in Co(II) complex at 215nm, 245nm and 251nm which were assigned to 4T1g→4T1g, 4T1g→4T2g and 4T1g→4A2g within the octahedral geometry (Chudhary et al., 2017).

Antibacterial Activity

The antibacterial activity test results for both the ligand and metal complex are presented in Table 5.

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

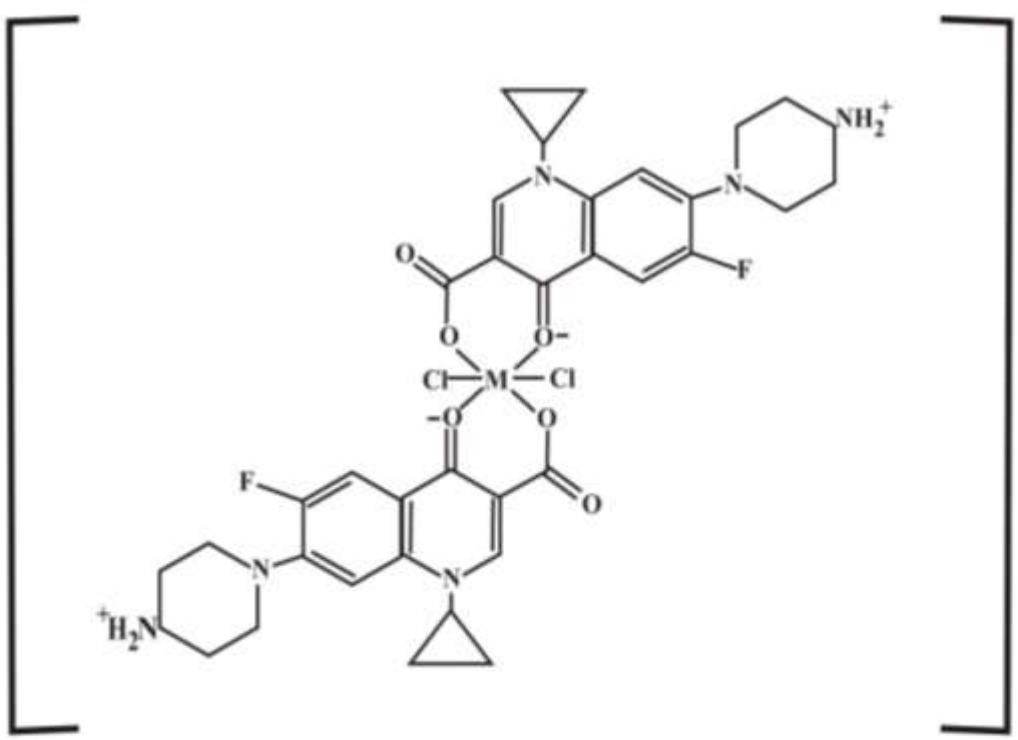
Compounds	Concentration (µg/ agar-well)	Inhibition Zones S. aureus (mm)	E. coli (mm)	S. typhi (mm)
Ciprofloxacin	5	13	15	18
	10	17	20	19
	20	24	25	22

[$Co(Cip)_2Cl_2$]	5	27	10	23
	10	31	14	29
	20	37	20	38
Standard (Gentamycin)	20	27	37	44

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

Ciprofloxacin complexes are all active against bacteria isolates. In general, these results revealed that the complex synthesized showed significant antibacterial strength even at low concentration as 5μ/agar-well in which the inhibitory action increases with increase concentration, these values are compared with the standard of Gentamycin which is similar with the result reported by (Mustapha et al., 2014).

From the spectral data obtained as well as the results from elemental analysis, molar conductivity and magnetic moment, the tentative proposed structure for the metal (II) complex of the ciprofloxacin as:



Proposed structure of Ciprofloxacin Complexes (M= Co^{2+})

Conclusion and Recommendations

Conclusion

Based on the above results obtained, the metal ion coordinated to the ligand through the ring carbonyl oxygen and one of the atoms of the carboxylate group given rise to octahedral geometry. The elemental analysis data also agreed with the proposed structure. Form the antibacterial activity of the complex, it shows the increase compare with the free ligand ciprofloxacin. Therefore, the result obtained for mechanochemical synthesis will help to minimize the use of more harmful solvents.

Recommendation

- This research work demonstrated the merit of mechanochemistry over solution-based synthesis as this call for scientist all over the world to exploit this wonderful synthetic method for the preparation of complexes and other compounds.
- The products obtained mechanically are comparable to those obtained via solution-based and have the advantage of producing fast, with higher yield, low cost and eco-friendly.
- The result obtained help to minimize the usage of harmful solvents.

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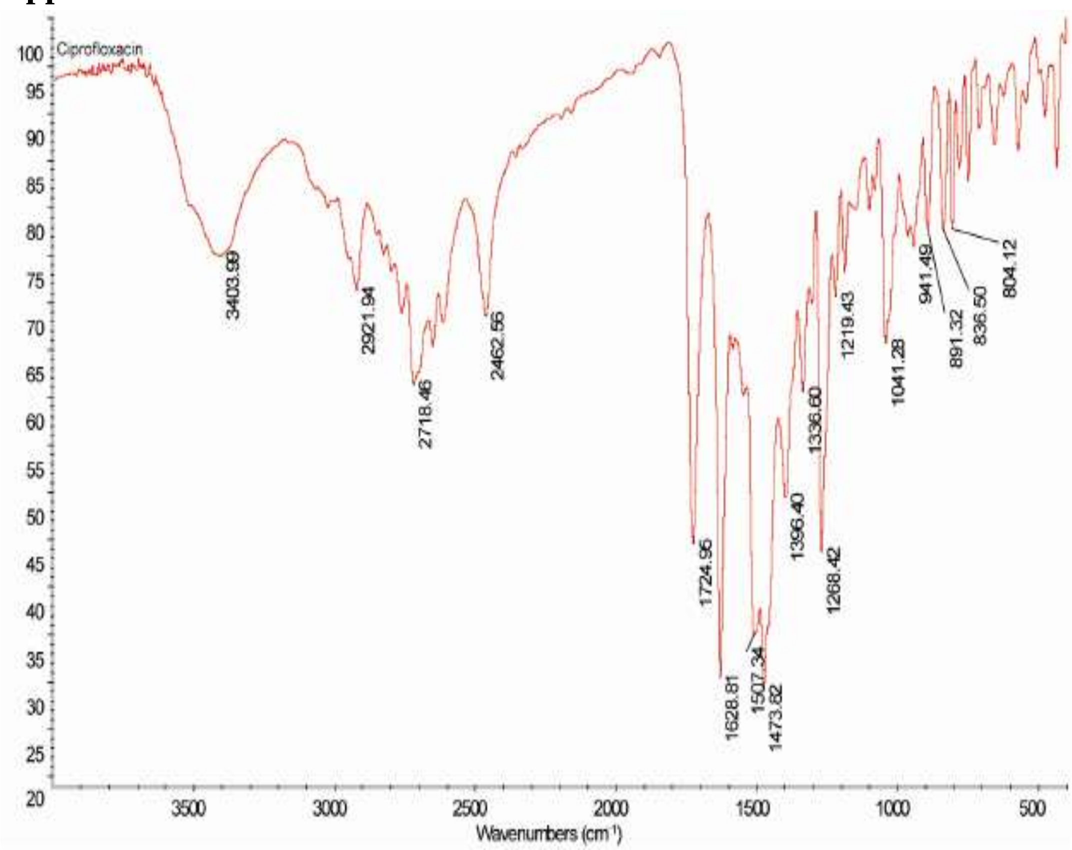
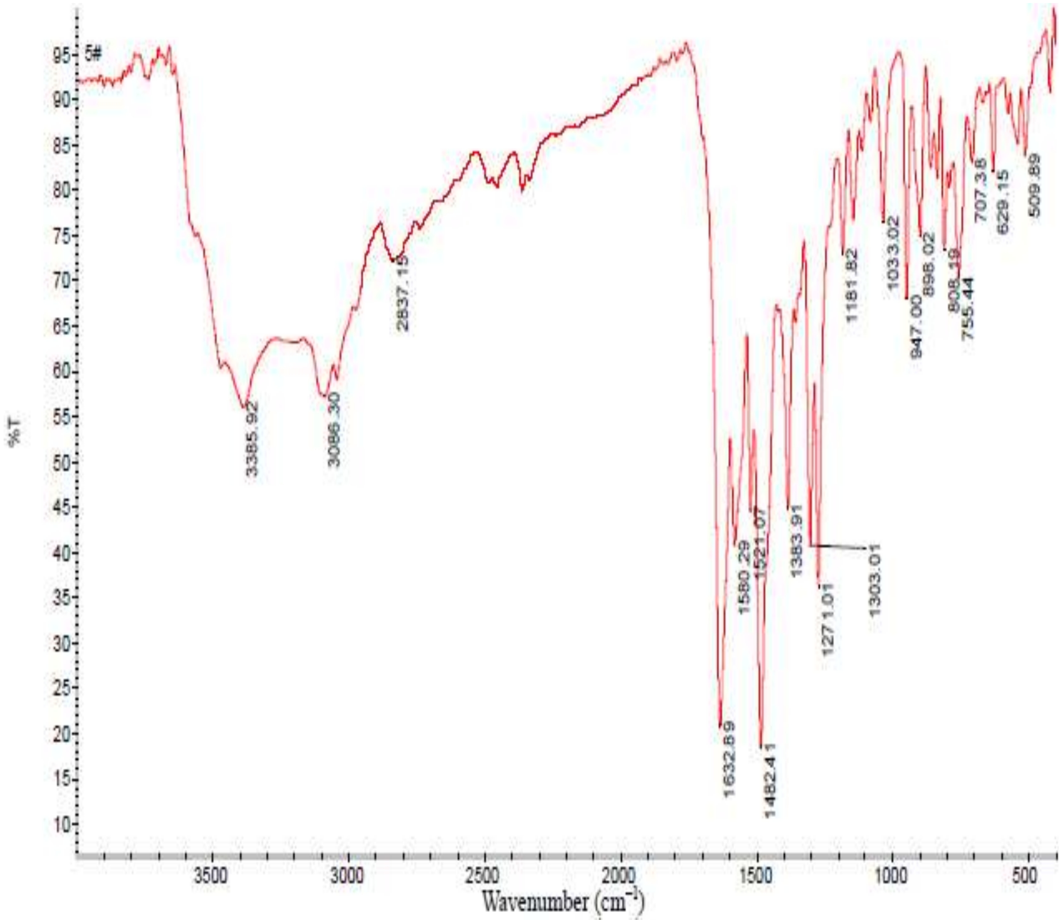
Appendix 1



IR Spectra of ciprofloxacin

Appendix 2



IR Spectra of Co (II) ciprofloxacin Complex