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Mechanochemical Synthesis and Characterization of Fe (II), Co (II), and Ni (II) Complexes Derived from Paracetamol

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Abstract

Solid-state synthesis of metal (II) complexes with paracetamol (ligand) was performed mechanically in a 1:2 ratio. The complexes have been characterized. From the IR and electronic spectral studies, the spectra of the complexes were different from that of ligands suggesting the formation of coordinations compound. Paracetamol was found to be bidentate ligand in which metal (II) complexes coordinated through the oxygen atom of carbonyl of ketone and the nitrogen atom of amide in which the complexes are assumed to have octahedral geometry. The melting point temperature of the ligand at 174.2^{0}C shows that it is stable at low temperatures while the decomposition temperatures of Fe, Ni, and Co complexes respectively at 229^{0}C, 245^{0}C, and 237^{0}C show that they are stable. The conductivity measurement shows that the complexes were found to be non-electrolytic as compared with the theoretical values. The suggestion of the complexes can also be provided by their magnetic moment, in which magnetic susceptibility studies proved that all the synthesized complexes are paramagnetic. The paracetamol and its complexes are soluble in DMSO, and insoluble in ethanol and distilled water. Paracetamol is a very interesting ligand and so many researchers synthesized such as using solution-based synthesis. This work has demonstrated the use of a solid-state method (a reliable method) to obtain the same result.

Keywords: Characterization, Schiff Base, Synthesis, Mechanochemical

Introduction

Mechanochemical refers to reactions, normally of solids, induced by the input of mechanical energy, such as by grinding in ball mills (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 Mechanochemical could in the future become a more mainstream technique for 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 about solvent production purification and recycling (James *et al*., 2012).

Solvents can be present in solid starting materials such as in hydrated metal salts or molecular solvates. There may even be (smaller) amounts of moisture in non-formally hydrated materials or in the atmosphere which aid the reaction. In experimental conditions, it is advantageous to add a few drops of solvent to the solids leading to so-called liquid-assisted grinding (LAG). In some cases, chemical reactions can also be initiated between a solid reactant and a liquid: in that case, the process is called kneading (Dubois *et al*., 2014). This research work is aimed at synthesizing characterizing metal (II) complexes of paracetamol via mechanochemical means. objectives of this research include; an alternative synthetic route for the synthesis of Ni (II), Co (II), and Fe (II) complexes of a and characterizing them by Solubility, Melting/decomposition temperature, Conductive measurement, Magnetic susceptibility measurement, and Infrared spectral analysis. It also includes determining the antimicrobial activity of metal (II) complexes of paracetamol to establish how metal-drug binding influences the activity of these drugs.

Mechanochemistry is concerned with the chemical reactions and structural changes induced by mechanical energy (Michalchuk *et al.*, 2012). In the modern world, many industries embrace this technology including mining, building, and pharmaceutical manufacturing sectors (Balaz P. 2008). The first systematic investigation of mechanochemistry was conducted in the nineteenth century and mechanochemistry was recognized as a branch of chemistry by Wilhelm Ostwald around the turn of the twentieth century. Since then the discipline has made steady progress. However, it is due to its aspects of green chemistry that mechanochemistry has seen a recent resurgence (Wieczorek *et al., 2012)*. The advancement of modern technology realized different types of high-energy ball mills with mechanical energy output (energy density) high enough to induce many chemical reactions. As such in mechanochemistry ball mills are often utilized as a chemical reactor. Because of this reason mechanochemical processing is also called ‘reactive milling (McCormick *et al.,* 1998). Attrition mills, planetary mills, and shaker mills are common types of mills used in mechanochemistry. The former two types of mills are also used for the commercial large-scale production of metal-oxide nanoparticles. The mechanisms to mechanically activate chemical reactions have been the subject of many studies. Mechanical energy input repeatedly causes the shifts of atoms from the equilibrium stable positions and in turn the changes of bond lengths and angles, and, in some cases, the excitation of electron subsystems (Tkacova *et al.,* 2016). This leads to the creation of defects, and amorphization/metastable phases to accumulate energy that is released to rapture chemical bonds and causes chemical reactions. However, the detailed study of the mechanochemical activation during ball milling is not straightforward because of the short duration of each collision event and the localized character of the event in terms of heat and pressure. Nevertheless, in situ measurements have been attempted and thermodynamical analyses and kinetic modeling have been conducted to understand the reaction processes. A wide variety of materials have been produced using Mechanochemical processing (Boldyreva *et al.,* 2013). They include metals and their alloys, oxides and other chalcogenides, refractory materials such as carbides and silicides, and common salts such as carbonates and phosphates (Tan & Garcia 2019). The ability of mechanochemical processing is not limited to the synthesis of inorganic materials. Metal-organic frameworks, organometallic complexes organic compounds can also be produced using mechanochemistry. Moreover, the production of complex structures, such as hybrid materials consisting of a core of inorganic materials and a shell of organic materials was demonstrated by Mechanochemical processing (Shkhtshneider *et al.,* 2014). The usefulness of Mechanochemical processing to produce nano-structured materials was also recognized at an early development stage of nanotechnology. This research work is aimed at synthesizing and characterizing Schiff base and its metal (II) complexes of Iron, Cobalt, and Nickel derived from Paracetamol via the mechanochemical method.

Materials and Methods

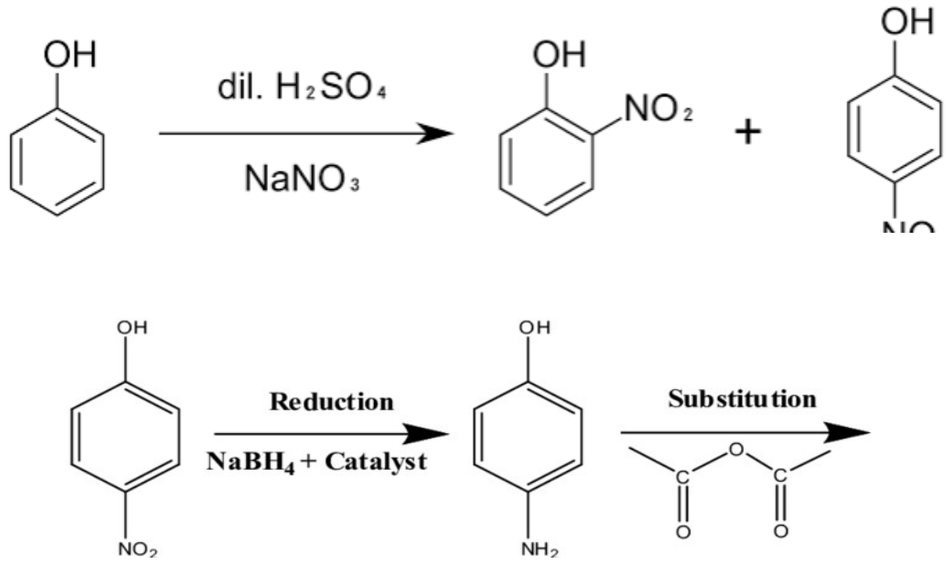
Material

All chemicals used were of analytical reagent grade (AR) and were used without further purification.

Methods

Synthesis of Paracetamol

In a small-scale laboratory, paracetamol is prepared by a three reaction Sequence. First nitration of phenol with sodium nitrates gives a mixture of two isomers, from which the wanted 4-nitro phenol can easily be separated by steam distillation. In this electrophilic aromatic substitution reaction, phenol's oxygen is strongly activating, thus the reactions required only mild conditions as compared to the nitration of benzene itself. The nitro group is then reduced to an amine, given 4-amino phenol. This reaction can be accomplished using sodium borohydride. Finally, the amine is acetylated with acetic anhydride. (Ellis *et al*, 2002).



Scheme 1: Synthesis of paracetamol

Synthesis of the Metal (II) Complexes

2.0g of the ligand (paracetamol) and 1.0g of (iron (II) chloride, Cobalt (II) chloride and Nickel (II) chloride) were ground separately using a glass mortar and pestle. Diethyl ether (as LAG) was added in two drops and grounded for 15 minutes until a clear brown powder colour complex (Scheme 2), pink powder colour complex (Scheme 3), and light green powder colour complex (Scheme 4) were obtained respectively which was Recrystallized using diethyl ether

.

$$\mathbf{FeCl_2.4H_2O + 2para} \xrightarrow{\text{Grinding } (C_2H_5O)_2O} \mathbf{[Fe(para)_2Cl_2]}$$

Scheme 2: Solid state synthesis of [Fe (para)$_2$Cl$_2$]

$$\mathbf{CoCl_2.4H_2O + 2para} \xrightarrow{\text{Grinding } (C_2H_5O)_2O} \mathbf{[Co(para)_2CL_2]}$$

Scheme 3: Solid state synthesis of [Zn(para)$_2$CL$_2$]

$$\mathbf{NiCl_2.4H_2O + 2para} \xrightarrow{\text{Grinding } (C_2H_5O)_2O} \mathbf{[Ni(para)_2Cl_2]}$$

Scheme 4: Solid state synthesis of [Ni(para)$_2$Cl$_2$]

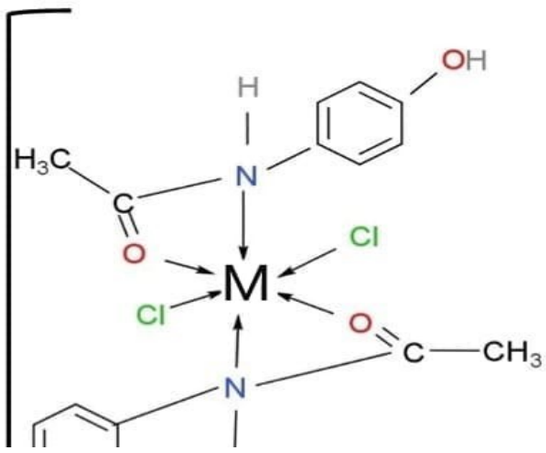


Fig. 1: Proposed structure of the metal (II) complexes
Where M = Fe, Co and Ni

Solubility test

The solubility of the Schiff base and its metal (II) complexes were determined in different solvents ranging from polar to non-polar such as distilled water, methanol, ethanol, ester, acetone, diethyl ether, Aldehyde and dimethyl sulphoxide (DMSO). In 0.1 g of each sample was tested in 10 ml of each solvent. Kurawa and Yammama (2014)

Fourier transform Infrared Spectroscopy (FTIR)

The Schiff base and its metal (II) complexes synthesized were subjected to IR testing and characterized. FT-IR spectra were recorded in the range of 400 = 4000 cm-1 using FT-IR by Agilent Technologies at Instrumental and central laboratories Umaru Musa Yar'adua University Katsina, Nigeria

Magnetic susceptibility

The Synthesized metal (II) complex was introduced into the balance's capillary tube up to a given mark and the reading was recorded using the magnetic susceptibility balance of Sherwood Scientific Cambridge UK. The formula below was used to calculate the magnetic susceptibility (Xg). That is

$$Xg = \frac{CXLC(R_1-R_0)}{10^9XM}$$

$Xm = Xg \times fw$ (g/mol)

NOTE: Where C =Constant of proportionality (1.0)

MSB- Magnetic susceptibility balance

M – Mass of a sample

R – MSB reading obtained for tube + sample

R0 – MSB empty tube reading (normally negative value)

W1 – Weight of empty capillary tube by analytical balance (mg)

W2 – Weight of capillary tube + sample by analytical balance (mg)

Melting points

The Melting point of the ligand as well as the decomposition temperatures of the complexes were determined by introducing a pinch of each sample into a capillary tube and then inserted into the Stuart melting point apparatus (SMP 10), the temperature at which the ligand melts and the complexes decomposed were recorded. Similar to the report of (Waziri *et al.,* 2017).

Molar conductance

Molar conductance of the ligand and the complexes was carried out in dimethyl sulphoxide (DMSO) by dissolving 0.001g of each sample in 10 ml of the solvents in a test tube the test was carried out using a conductivity meter of model DSS-307 in 1x10-3 DMSO at chemistry laboratory federal University Dutsin-ma. the electrode was inserted and the reading was taken. The results obtained were compared with the one reported by (Mustapha et al., 2014).

Results and Discussions

Results

The results obtained from various analyses in this research are presented in the following Tables

Table 1: Physical properties of paracetamol and its metal (II) complexes

Compound	Colour	Melting point (^{0}C)	Decomposition Temperature (^{0}C)
Paracetamol	White	174.2	-
[Fe(para)Cl_2]	Brown	-	229
[Ni(para)Cl_2]	Light green	-	245
[Co(para)Cl_2]	Blue	-	237

Table 2: Solubility of Paracetamol and its metal (II) complexes

Compound	Ethanol	Methanol	DMSO	Ester	Acetone	Aldehyde	Diethyl ether	Distilled water
Paracetamol	IS	IS	S	IS	SS	IS	SS	IS
[Fe(para)Cl_2]	IS	IS	S	SS	IS	SS	IS	IS
[Ni(para)Cl_2]	IS	SS	S	SS	SS	S	IS	IS
[Co(para)Cl_2]	IS	SS	S	SS	SS	SS	IS	IS

Key: S = soluble, IS = insoluble and SS = slightly soluble

Table 3: Molar conductance in DMSO solvent

Compound	Molar conductivity (MS/CM)
Paracetamol	0.00
[Fe(para)Cl_2]	0.71
[Ni(para)Cl_2]	2.36
[Co(para)Cl_2]	0.57

Discussion

The interaction of paracetamol and metal complexes resulted in the formation of different colours, the ligand paracetamol melted with a melting point temperature of 174.2ºC. The interaction of paracetamol with respective divalent metal salts yields coloured complexes, the colour of the complexes is due to the electronic transition from lower to higher energy levels. Iron, Cobalt, and Nickel complexes are brown, light green, and blue colour with decomposition temperatures of 229ºC, 245ºC, and 237ºC respectively, the high decomposition temperature of the complexes as compared to the ligand may be due to the coordination between the central metal ion and the ligands. (Table 1). From Table 3 both paracetamol and its complexes are soluble in DMSO, and insoluble in ethanol and distilled water. Other organic solvents such as methanol, ester, acetone, Aldehyde, and diethyl ether are soluble, slightly soluble, and insoluble. This agreed with the saying "like dissolves like". The molar conductance in $1x10^{-3}$ DMSO is presented in Table 3. Conductivity measurements have frequently been used in elucidating the structure of complexes within the limit of their solubility in a particular solvent Paracetamol, [Fe(para)Cl_2], [Ni(para)Cl_2] and [Co(para)Cl_2] complexes have a molar conductance value of 0.00MS/CM, O.71MS/CM, 2.36MS/CM and 0.57MS/CM respectively, which indicate that they are non-electrolyte.

The suggestion of the complexes can also be provided by their magnetic moment, in which

magnetic susceptibility studies proved that all the synthesized complexes are paramagnetic as shown in Table 4. The FT IR data of the ligand and its complex are presented in Table 5. The bands at 1654 cm^{-1} and 1222 cm^{-1} for the ligand are assigned to ν(C=N) cm^{-1} and ν(C-O) cm^{-1} respectively. For [Fe(para)Cl_2] the bands at 1651 cm^{-1}, 1272 cm^{-1},521 cm^{-1},432 cm-1, and 3406 cm^{-1} are assigned to ν(C=N) cm^{-1} ,ν(C-O) cm^{-1},ν(M-N) cm^{-1},ν(M-O) cm^{-1} and ν(H-O) cm^{-1}respectively. For [Ni(para)Cl_2] the bands at 1615 cm^{-1}, 1256 cm^{-1}, 576 cm^{-1}, 487 cm^{-1} and 3160 cm^{-1} are assigned to ν(C=N) cm^{-1} , ν(C-O) cm^{-1},ν(M-N) cm^{-1},ν(M-O) cm^{-1} and ν(H-O) cm^{-1}respectively. For [Co(para)Cl_2] the bands at 1653 cm^{-1}, 1286 cm^{-1}, 541 cm^{-1}, 453 cm^{-1} and 3324 cm^{-1} are assigned to ν(C=N) cm^{-1} ,ν(C-O) cm^{-1}, ν(M-N) cm^{-1},ν(M-O) cm^{-1} and ν(H-O) cm^{-1} respectively. Comparing the bands in the ligand to that of the metal complexes shows that the ligand has coordinated with the metal salt in 1:2 ratios

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Table 4: Laboratory Balance for Magnetic Susceptibility

SAMPLE ID	M(mg)	L(cm)	R	R_0	W_1	W_2	Xg	Xm(g/mol)	Property
[Fe(para)Cl_2]	87	3.00	270	-025	655	742	0.093	19.16	Paramagnetic
[Ni(para)Cl_2]	106	3.00	570	-025	655	761	0.171	35.94	Paramagnetic
[Co(para)Cl_2]	136	3.00	150	-025	655	791	0.031	6.51	Paramagnetic

NOTE: Where C =Constant of proportionality (1.0), MSB- Magnetic susceptibility balance, M – Mass of a sample
R – MSB reading obtained for tube + sample, R_0 – MSB empty tube reading (normally negative value)
W_1 – Weight of empty capillary tube by analytical balance (mg), W_2 – Weight of capillary tube + sample by analytical balance (mg)

Table 5: The IR spectra (4000-400 cm^{-1}) of paracetamol and its metal (II) complexes

Compound	ν(C=N)cm^{-1}	ν(C-O)cm^{-1}	ν(M-N)cm^{-1}	ν(M-O)cm^{-1}	ν(H-O)cm^{-1}
Paracetamol	1654	1222	-	-	-
[Fe(para)Cl_2]	1651	1272	521	432	3406
[Ni(para)Cl_2]	1615	1256	576	487	3160
[Co(para)Cl_2]	1653	1286	541	453	3421

Conclusion

Paracetamol is a very interesting ligand and so many researchers synthesized such as using solution-based synthesis. This work has demonstrated the use of a solid-state method (a reliable method) to obtain the same result. From the values obtained in spectral studies, conductivity and magnetic measurement suggested octahedral geometry. In the spectral studies of the IR Spectroscopy the ligand is coordinated with the metal ion to form a complex of [Fe(para)Cl_2], [Ni(para)Cl_2] [Co(para)Cl_2] through υ(C =O) and υ(N-H) of amide given rise to octahedral geometry.

Recommendations

This research work encourages the importance of the solid-state method over solution-based synthesis for the production of metal (II) drug complexes because it gives a higher yield, promotes reactions very quickly, is cost-effective, reduces environmental contamination, etc. Mechanochemical synthesis needed to be modernized by making it an easier way to grind the metal salt with ligands without using mortar and pestle. It was recommended that elemental analysis should be done on the synthesized compounds. It was also recommended that Anti-microbial analysis should be done on the synthesized compounds

References

Abidallah A,. Babamale, HF; Lawal, A; Rajee, OA; Oloyede, EA. (2011*). Synthesis, Characterization and Biological Activity Studies of Schiff base Metal Complexes.*Vol. 20 (4) 1157-1161.

Ammar, A. A., Samaa, A. R., Waseen, M., Gamel, H., & Sheik, M.S. (2021). Preparation of new complexes from a mixture of aspirin (acetylsalicylic acid), Paracetamol, and methyldopa with divalent manganese, iron, cobalt, nickel, and copper with a study of their physical and chemical properties. Egyptian *Journal of Chemistry. 64*(5): 2405-2413.

Baláž, P. (2008) Mechanochemistry in Nanoscience and Minerals Engineering. (Springer-Verlag,)

Boldyreva, E. *Mechanochemistry of inorganic and organic systems: what is similar, what is different?* Chem.Soc. Rev. 42, 7719–7738 (2013).

Byrantet dombee b., arturo robertazzi æ james a. platts (2007). Despite the evidence that paracetamol and NSAID have some similar pharmacological activity and classification of paracetamol. *biol inorg chem 10: 854–866.*

Dubois, J., Colaco, M. O., & Wouters, J. (2014). *Mechanosynthesis, a method of choice in solid-state synthesis,* 117, 21-30.

Dubois, J., Colaco, M., & Wouters, J. (2014*).Mechanosynthesis, a method of choice in solid state synthesis*: 21-30.

Ellis B.,Nattaya T, Pinya M, Ruangdaj T. (2012*).* Synthesis of paracatemol*Journal of Natural Sciences 16(4):239-253*

Goes, A. (2020). *Discussion and conclusion. To access the antimicrobial action of paracetamol*, 68.

James, S. L., Adams, C. J., Bolm, C., Braga, D., Collier, P., Frinsic, T., … & Grepioni, F.(2012*).Mechanochemistry Oppurtunity for new and cleaner Synthes Chemical Society Reviews*, 14(1), 413-447

Klebsiellaet A.B., Olagboye S.A., Adekeye D.K. and Akinwunmi O.A. (2016*). Antimicrobial activities of novel synthesized cu (ii) and co (ii) mixed ligand complexes of prednisolone and paracetamol*. Volume 10, Issue 3, March-2019 651 ISSN 2229-5518. https://www.researchgate.net/publication/344429477

Kuboto, J. K., Willian, K., Rifs, M. A., & Rusev, L. K. (2019). Formation of metformin complexes with some transition metal ions and their biological activity. *Journal of health care, 6*(3), 19 – 28.

McCormick, P. G. & Froes, F. H. The fundamentals of mechanochemical processing. *J. Miner., Met. Mater. Soc*. 50,61–65 (1998).

Michalchuk, A. A. L., Boldyreva, E. V., Belenguer, A. M., Emmerling, F. & Boldyrev, V. V. Tribochemistry, mechanical alloying, mechanochemistry: what is in a name? Front. Chem. 9, 685789 (2012).

Mukhtar A. Kurawa, Jamilu Jaafar, (2021). Solid State Synthesis, Characterization and Anti-Microbial Studies of some Transition Metal Complexes of a Schiff Base Ligand Derived from Benzophenone and Glycine. *ChemSearch Journal* 12(1): 41 – 46. ISSN: 2276 – 707X. http://www.ajol.info/index.php/csj

Paracetamol: *WilipediA*. (n.d). retrieved November Sunday, 2021, from Wikipedia: en.m.wikipedia.org/wiki/paracetamo

S. Jibril1, K. A. Baraya, S. Muhammad, I. Musa, A. Garba1, S. B. Adamu, and I. Bello. (2021).Solid-state synthesis, spectral and biological studies of fe (ii) complex derived from paracetamol. *J. Chem. Soc. Nigeria,* Vol. 46, No. 6, pp 1068 – 1074

Sadia Afrin Dalia, Farhana Afsan, Md. Saddam Hossain, Md. Nuruzzaman Khan, CM Zakaria, Md. Kudrat-E-Zahan and Md. Mohsin Ali. (2016).A short review on the chemistry of Schiff base metal complexes and their catalytic application. *International Journal of Chemical Studies* 2018; 6(3): 2859-2866**.** https://www.researchgate.net/publication/325845095

Shakhtshneider, T. P., Myz, S. A., Boldyreva, E. V., Nizovskii, A. I. & Kumar, R. (2014). Core-shell *mechano-composites of drugs with inorganic oxides and hydroxides*. Acta Phys. Polonica A 126, 1019–1024

Tan, D. & García, F. (2019). Main group mechanochemistry: from curiosity to established protocols. *Chem. Soc. Rev*. 48, 2274–2292

Tkáčová, K., Heegn, H. & Števulová, N. Energy transfer and conversion during comminution and mechanical activation. *Int. J. Miner. Process.* 40,17–31 (1993). 15. Boldyrev, V. V. Mechanochemistry and mechanical activation of solids. Russian Chem. Rev. 75, 177–189 (2006).

Waziri, I., Mala, G. A., Fugu, M. B., Isa, B., & Umaru, U. (2017). *Synthesis, spectral Characterization and antimicrobial.*

Wieczorek-Ciurowa, K. & Gamrat, K. (2012) Mechanochemical syntheses as an example of green processes. *J. Therm. Anal. Calorim*. 88, 213–217