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### XRD and spectroscopy analyzes of 4-acetamidophenol grown by single diffusion gel method

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#### ABSTRACT

Another name of 4-acetamidophenol is popularly known as the paracetamol. It was considered as one of the safest and most frequently used analgesic and antipyretic drug all over the world. This medicinal important drug compound was grown by the single diffusion gel method for the first time to improve the quality of the crystal. The harvested crystals are analyzed by powder XRD, FT-IR and UV-Visible spectroscopy studies. The powder XRD study confirms the crystallite compound of 4-acetamidophenol by comparing  $2\theta$  and  $d$ -spacing values of the compound with JCPDS values of the same compound. The functional groups present in the molecule and their wavenumber assignments were made in the FT-IR spectroscopy study. The optical band gap and the transparency of the grown crystals are found by using the UV-Visible spectroscopy study.

**Keywords:** 4-acetamidophenol, single diffusion gel method, XRD, FT-IR, UV-Visible spectroscopy.

#### INTRODUCTION

4-Acetamidophenol (Paracetamol) is used as one of the safest and most frequently used medicine in all around the world. It is consider as a mild painkiller and reduces the temperature of patients with fever. These actions are known as analgesic and antipyretic respectively. The 4-acetamidophenol is also used to manage the post-surgical and cancer pain [1-3]. However; it had a serious side effect involving the deactivation of some of the hemoglobin in red blood cells. Ingestion of paracetamol in young children may cause asthma, eczema, and allergic rhinitis in early life of some children [4-6]. This pharmaceutical compound of 4-acetamidophenol has three polymorphisms [7, 8]. These are stable monoclinic (Form I), meta stable orthorhombic (Form II) and unstable Form III (not yet characterized). Most of the paracetamol drug samples belong to monoclinic form which is the most stable polymorph [9]. Many authors report the preparation of single paracetamol crystals by the solvent evaporation technique [10, 11] with a seed. The crystal structure of paracetamol has been studied by many researchers [12, 13]. In this present work, the crystals of 4-acetamidophenol was grown by the single diffusion gel method. The crystals are grown within 3-5 weeks in this method. The harvested crystals were characterized by the single crystal XRD, Powder XRD, FT-IR, UV-Visible spectroscopy studies.

#### MATERIALS AND METHODS

##### Materials

The materials used for this crystallization are 4-acetamidophenol (98 % Alfa Aesar) was purchased from Johnson Matthey company and sodium silicate, ethanol, acetic acid (99.5 %) were purchased from the Merck, India.

**Single Diffusion Gel Method**

The title compound was crystallized by the single diffusion gel method. At first the Silica gel was created by mixing an aqueous solution of 1 M sodium meta silicate with 1M acetic acid. These solutions are stirred continuously by the magnetic stirrer to avoid the pre local gel formation. Then the mixture was transferred into the test tube of length 15 cm and 3 cm diameter. The mouth of the test tube was covered by the cork to keep the solution free from dust and impurities. The gel was set within the 2 or 3 days and leaves it for another 24 hours for aging. Then the aqueous ethanol solution of 4-acetamidophenol (1M) was poured slowly over the set gel without disturbance. The colorless crystals were appeared within the two days in the gel medium which are harvested after 3–5weeks and washed with the distilled water. The crystals were collected and dried crystals were stored in the clean container. The photographic view of the grown crystals is shown in fig.1. The optimum conditions used in the crystal growth of this method are given in Table 1.

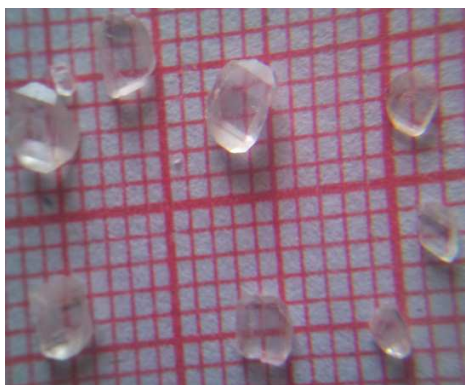


Figure 1: Photographic view of 4-acetamidophenol crystals

Table 1: The optimum conditions for grown crystals of 4-acetamidophenol

Parameters	Optimum conditions
Density of sodium meta silicate	1.06 g/cm <sup>3</sup>
Concentration of acetic acid	1 M
Concentration of 4-acetamidophenol	1 M
pH of the gel	4.8
Gel setting period	2 days
Gel aging	24 hours
Period of growth	3–5 weeks
Temperature	Room temperature

**RESULTS AND DISCUSSION****Characterization**

The title compound of 4-acetamidophenol was analyzed by the powder XRD, FT-IR and UV-Visible spectroscopy studies. The powder X-ray diffraction of the crystalline sample was carried out, using XPERT-PRO X-ray diffractometer with Cu K $\alpha$  ( $\lambda = 1.54060 \text{ \AA}$ ) radiation. The FT-IR spectrum of the sample was recorded by using SHIMADZU FT-IR Spectrometer in the range 4000–400 cm<sup>-1</sup>. The sample for this measurement was finally ground and mixed with KBr. The mixture was pressed under vacuum at very high pressure to obtain a transparent disc, which yield good spectra. The optical transmittance and absorbance spectrum of grown crystal has been recorded with SHIMADZU-UV1800, double beam spectrometer. Transmittance and absorbance data were observed for the title compound in the wavelength range 200–1100 nm insteps of 1nm. The slit width chosen was 1 nm. The wavelength rate was in medium mode. The observed values of absorbance were recorded and stored in the memory of a computer and plotted.

**Powder XRD Analyzes**

The X-ray powder diffraction patterns were collected for 4-acetamidophenol compound using a XPERT-PRO X-ray diffractometer with Cu K $\alpha$  ( $\lambda = 1.54060 \text{ \AA}$ ) radiation. The XRD pattern of the title compound is depicted in fig. 2. The  $2\theta$  and d-spacing values of 4-acetamidophenol are shown in Table 2 which are compared with JCPDS values (JCPDS card No. 39-1503) of the same compound. The form I and form II polymorphs of 4-acetamidophenol

can be distinguished by using this powder XRD study. The monoclinic (form I) and orthorhombic (form II) crystal systems of 4-acetamidophenol has the space group P2<sub>1</sub>/n and Pbc<sub>a</sub> respectively [14].

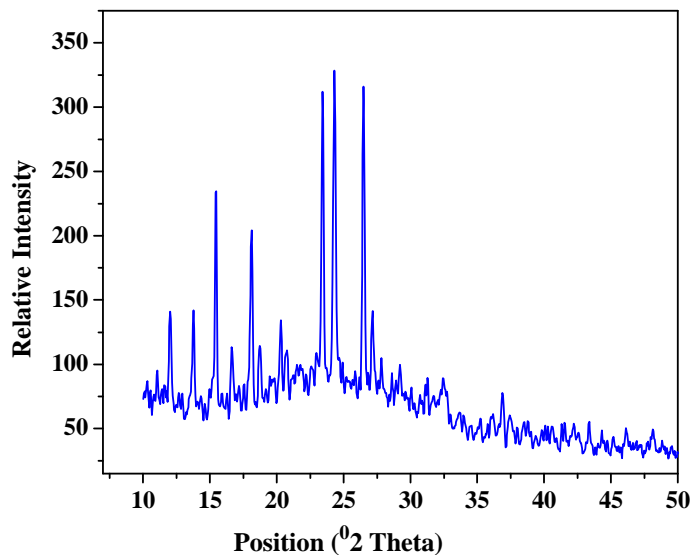


Figure 2: Powder XRD pattern of 4-acetamidophenol

Table 2: Powder XRD data of 4-acetamidophenol

Present Work		JCPDS file (39-1503)		
Position [°2θ]	d-spacing [Å]	Position [°2θ]	d-spacing [Å]	(hkl)
12.0241	7.36068	12.124	7.3000	$\bar{1}10$
13.7664	6.43274	13.819	6.4080	$\bar{1}01$
15.4492	5.73565	15.529	5.7060	101
16.6462	5.32579	16.759	5.2900	$\bar{1}11$
18.1070	4.89930	18.208	4.8720	111
18.7276	4.73833	18.909	4.6930	020
20.3169	4.37111	20.430	4.3470	$\bar{1}20$
23.4317	3.79664	23.510	3.7840	$\bar{1}21$
24.3134	3.66091	24.392	3.6490	$\bar{2}20$
26.4789	3.36622	26.551	3.3570	$\bar{3}11$
27.1284	3.28709	27.186	3.2800	$\bar{1}12$
32.5044	2.75467	32.529	2.7530	$\bar{2}30$
36.8819	2.43715	36.945	2.4330	$\bar{3}30$

The powder XRD data of title compound is exactly coinciding with the JCPDS values of the same compound. The cell parameter values of the 4-acetamidophenol crystal are tabulated in Table 3 which is taken from the JCPDS file.

Table 3: Cell parameter values of 4-acetamidophenol

a= 11.72 Å
b =9.379 Å
c = 7.106 Å
$\alpha = 90^\circ$
$\beta =97.472^\circ$
$\gamma = 90^\circ$
space group=P2 <sub>1</sub> /n
crystal system= Monoclinic
V =774.89 Å <sup>3</sup>
Density =1.296 g/ cm <sup>3</sup>

The XRD diffraction results indicate that the grown crystal of 4-acetamidophenol by the gel method has the stable polymorph form I of monoclinic. The molecular structure of 4-acetamidophenol is depicted in fig. 3.

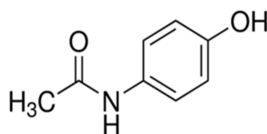


Figure 3: Molecular structure of 4-acetamidophenol

#### *FT-IR Spectroscopy Analyzes*

The 4-acetamidophenol molecule containing the three fundamental functional groups that is, benzene ring, amide (HN-CO-CH<sub>3</sub>) and hydroxyl (O-H) groups. The experimental FT-IR spectrum of title compound is shown in fig. 4. The detailed wavenumber assignment in FT-IR spectrum of 4-acetamidophenol is given in Table 4.

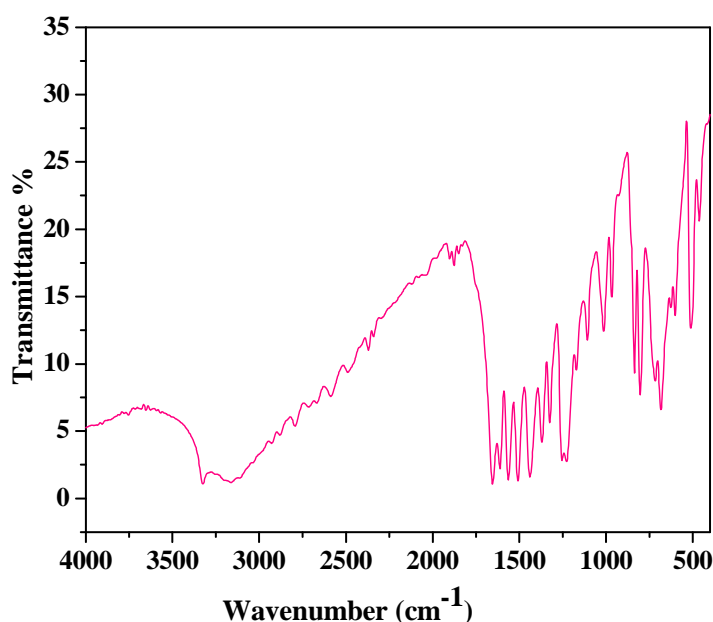


Figure 4: FT-IR spectrum of 4-acetamidophenol

#### *Aromatic Ring Vibrations*

The most of the C-H stretching bonds of aromatic compounds have the infrared peaks in the region 3080–3010 cm<sup>-1</sup> [15]. Accordingly, the symmetric stretching vibration of the C-H group is assigned at 3050 cm<sup>-1</sup> in FT-IR spectrum of the title compound. The C-H in plane bending vibrations usually occurs in the region 1430–990 cm<sup>-1</sup> [15]. In this study, the FT-IR peaks at 1370, 1325, 1254, 1227, 1171, 1107 and 1015 cm<sup>-1</sup> are assigned to C-H in-plane-bending of C-H group. The aromatic out-of-plane C-H bending absorption bands occur between 900–690 cm<sup>-1</sup> regions [15]. In the present study, the peaks at 837, 804 and 718 cm<sup>-1</sup> in FT-IR confirm the C-H out of plane bending vibrations. The C=C ring stretching modes are observed between the region 1650–1430 cm<sup>-1</sup> [16]. This C=C aromatic stretching vibrations are noted for the title compound at 1612, 1564, 1508, 1439 cm<sup>-1</sup> in FT-IR spectrum. The expected range of C-C vibration is between 1400–1300 cm<sup>-1</sup> [16]. In the present work, it is assigned at 1439, 1370 and 1325 cm<sup>-1</sup>. These C-C stretching vibrations are coupled with skeletal ring (C=C) and in-plane bending C-H vibrations. The ring breathing mode is identified at 966 cm<sup>-1</sup> in the IR spectrum of the title compound.

#### *Amide Group Vibrations*

The amide N-H stretching band is observed at 3300–3250 cm<sup>-1</sup> and the bending of N-H group appears at 1560–1530 cm<sup>-1</sup>. A broad N-H wagging band also appears at 750–650 cm<sup>-1</sup> [17]. The N-H stretching and bending modes of amide group of 4-acetamidophenol are identified as the sharp intense peaks at 3325 cm<sup>-1</sup> and 1564 cm<sup>-1</sup> in the IR

spectrum. These wavenumbers are deviated from the expected range is due to the presence of other vibrations such as (C=O) and  $-\text{CH}_3$  vibrations as shown in molecular structure of 4-acetamidophenol (fig. 3). The N-H wagging mode is observed at 718, 685  $\text{cm}^{-1}$  in the IR spectrum. Also the C-N stretching vibration of secondary aromatic amide absorb strongly at 1342-1320 and 1315-1250  $\text{cm}^{-1}$  in the IR spectrum [16]. The title compound absorbs the bands at 1325  $\text{cm}^{-1}$  and 1254  $\text{cm}^{-1}$  in the FT-IR spectrum for C-N stretching vibrational mode.

Table 4: Observed wavenumbers in FT-IR spectrum and their assignments for 4-acetamidophenol

Wavenumber FT-IR ( $\bar{\nu}$ / $\text{cm}^{-1}$ )	Assignment
3325 (s)	$\nu$ N-H
3163 (br)	$\nu$ O-H
3050 (w)	$\nu$ C-H
2950 (w)	$\nu_{\text{as}}$ - $\text{CH}_3$
2880 (m)	$\nu_{\text{s}}$ - $\text{CH}_3$
1655 (s)	$\nu$ C=O
1612 (m)	$\nu$ C=C
1564 (s)	$\nu$ C=C + $\delta$ N-H
1508 (s)	$\nu$ C=C
1439 (s)	$\nu$ C-C + $\beta$ O-H
1370 (m)	$\nu$ C-C + $\beta$ C-H
1325 (w)	$\nu$ C-C + $\nu$ C-N
1254 (m)	$\nu$ C-C + $\nu$ C-N
1227 (m)	$\nu$ C-C
1171 (w)	$\nu$ C-C + $\rho$ - $\text{CH}_3$
1107 (w)	$\nu$ C-C
1015 (w)	$\nu$ C-C
966 (s)	Ring breathing
950 (sh)	$\gamma$ O-H
837 (s)	$\gamma$ C-H
804 (m)	$\gamma$ C-H
718 (w)	$\gamma$ C-H + $\omega$ N-H
685 (s)	$\gamma$ C-H + $\omega$ N-H

w-weak; s-strong; m-medium; sh-shoulder;  $\nu$ -stretching;  
 $\nu_{\text{s}}$ -sym. stretching;  $\nu_{\text{as}}$ -asym. stretching;  $\rho$ -rocking;  
 $\gamma$ -out-of-plane bending;  $\beta$ -in-plane bending;  
 $\delta$ -bending;  $\omega$ -wagging

In methyl group ( $-\text{CH}_3$ ), the C-H stretching mode has lower wavenumber than those of aromatic ring (3100–3000  $\text{cm}^{-1}$ ). Moreover, the antisymmetric stretch is usually observed at higher wavenumber side than the symmetric stretch. In this present work, the  $-\text{CH}_3$  symmetric stretching frequency is assigned at 2880  $\text{cm}^{-1}$ , whereas the antisymmetric stretching mode are assigned at 2950  $\text{cm}^{-1}$  in the FT-IR spectrum of 4-acetamidophenol. The deformation of  $-\text{CH}_3$  group is usually observed in the range 1450–1400  $\text{cm}^{-1}$  for methyl substituted aromatic rings [18]. Accordingly, the peaks at 1439  $\text{cm}^{-1}$  in FT-IR is assigned to  $-\text{CH}_3$  in-plane bending deformation vibrations and the peaks at 1171  $\text{cm}^{-1}$  (FT-IR) is assigned to  $-\text{CH}_3$  rocking modes for the title compound. The C=O stretching vibration is assigned in the literature as a very strong band at 1661  $\text{cm}^{-1}$  in FT-IR spectrum [19]. The C=O stretching mode of the title compound is found at 1655  $\text{cm}^{-1}$  in the FT-IR spectrum.

#### Hydroxyl Group Vibrations

The free  $-\text{OH}$  group of phenol absorbs a band at 3615  $\text{cm}^{-1}$  while the associated  $-\text{OH}$  group has a stretching wavenumber in the range 3250–3200  $\text{cm}^{-1}$  [18, 20]. In the present work, the broad bands occur at 3163  $\text{cm}^{-1}$  is attributed to the O-H stretching mode of the title compound. The O-H in-plane and out-of-plane bending wavenumber normally occurs in the region between 1440–1395  $\text{cm}^{-1}$  and 960–875  $\text{cm}^{-1}$  respectively [21]. In the present study, bands at 1439  $\text{cm}^{-1}$  and 950  $\text{cm}^{-1}$  in the FT-IR spectrum is assigned to the O-H in plane and out of plane bending wavenumber respectively.

#### Ultraviolet Visible Spectroscopy Analyzes

The UV-Visible spectroscopy analyzes is one of the most frequently employed techniques to analyze the pharmaceutical compound. The absorbance spectrum of 4-acetamidophenol is shown in fig. 5. The maximum absorbance wavelength ( $\lambda_{\text{max}}$ ) for 4-acetamidophenol crystal is found to be at 248 nm and the lower cut-off wavelength is observed at 302 nm.

From the absorbance spectrum the crystal shows the good transmittance in the entire range of visible region. The band gap of the crystal was estimated by using the following the relation [22].

$$E_g = \frac{1.243 \times 10^3}{\lambda_{max}}$$

The band gap value of the crystal was found to be as 5.01 eV. The high value of band gap indicates that the grown crystal may be act as a typical of dielectric material.

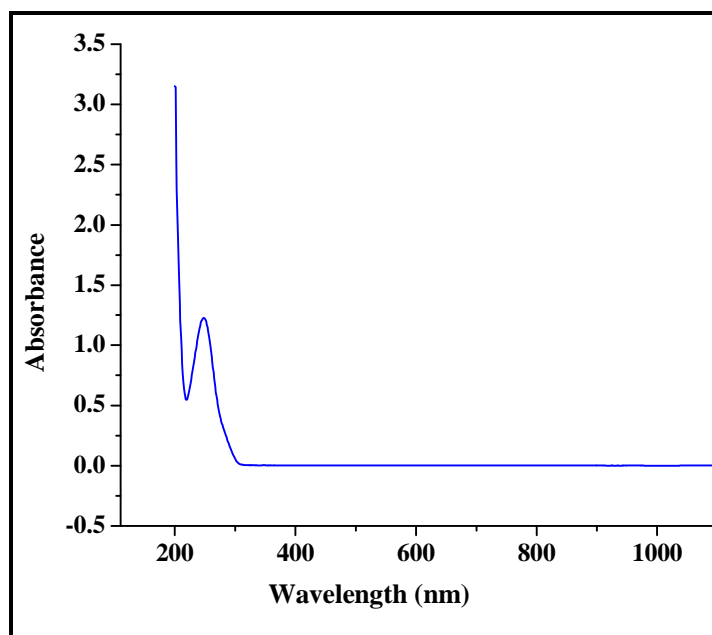


Figure 5: Absorption spectrum of 4-acetamidophenol

### CONCLUSION

The single crystals of 4-acetamidophenol were grown by using the gel method. The harvested colorless transparent crystals were carried out to the powder XRD, FT-IR and UV-Visible spectroscopy studies. The powder XRD study confirms the formation of 4-acetamidophenol crystal in the stable monoclinic form I. The monoclinic polymorph of 4-acetamidophenol was also one time confirmed by the FT-IR spectroscopy study by analyze the wavenumber assignment of functional groups present in the title compound. The UV-Visible spectroscopy study reveals the grown crystal may be under the typical of dielectric material. It was confirmed from the lower cut-off wavelength (302 nm) and the high value of band gap(5.01 eV) of 4-acetamidophenol pharmaceutical compound.

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