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Research Article

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Effect of EDTA on paracetamol drug

B. Kavitha[1], G. Madhurambal[2] and S. Nelson Amirtharaj[3]

[1]*Assistant Professor in Chemistry, TBML College, Porayar,-609307, Tamil Nadu, India*
[2]*Former Dean of Sciences and HOD of Chemistry, ADM College for Women, Nagapattinam- 611001, Tamil Nadu, India*
[3]*Assistant Professor in Chemistry, TBML College, Porayar-609307, Tamil Nadu, India*

ABSTRACT

In Pharmaceutical field, the search for compound that have suitable properties to be used in nowadays a big challenge, paracetamol, one of the most widely used drug is taken and the effect of dopant EDTA on the growth process, crystalline properties of paracetamol are investigated. The grown crystal was transparent, obtained within a period of few days. The grown crystal was subjected to various studies, such as X-Ray Diffraction(XRD), Fourier Transform Infrared (FTIR) and Ultraviolet-Visible (UV-Vis) absorbance, Thermogravimetric analysis and Differential thermal analysis (TGA/DTA). The functional groups of the crystals have been confirmed by FTIR analysis. The lattice parameters of the grown crystal were determined by single crystal XRD. A UV-Vis spectrum was recorded to find the suitability of the crystal for optical applications and band gap energy is determined. The thermal stability of doped crystal was checked using the TGA/DTA analysis. The surface morphology of the crystal was analysed by SEM and EDAX analysis was also carried out.

Keywords: Crystal growth, FTIR, Thermogravimetric analysis, UV-Vis, XRD

INTRODUCTION

In the last years, may leading pharmaceutical companies have begun to strictly control, the crystal chemistry of active pharmaceutical ingredients during their preparation and development stage. Crystals are the pillars of modern technology. Crystal of different materials has several applications. Paracetamol (PCT) is an acylated aromatic amide, which was firstly introduced into medicine as an antipyretic/analgesic by Von Mering in 1893 and has been in use as an analgesic for home medication for over 30 years and is accepted as an effective treatment for the relief of pain and fever in adults and children. PCT is also known as acetaminophen (N- acetyl – p- aminophenol, 4 – acetamidophenol); it is a major ingredient in numerous cold and flu medications and many prescription analgesics. In normal doses, PCT does not irritate the lining of the stomach or affect blood coagulation, the kidneys, or the fetel ductus arteriosus .Paracetamol is a widely used over-the-counter analgesic-antipyretic drug. Paracetamol is a weak prostaglandin inhibitor in peripheral tissues and possesses no significant anti inflammatory effects. EDTA can also be utilized in medicine. Doctors can prescribe EDTA treatments for patients suffering from lead poisoning. Such a treatment is known as chelation therapy, in which EDTA renders the toxic ions present in the body .[1-8]

EXPERIMENTAL SECTION

2.1. Preparation of solution

Exactly 0.5M solution is prepared by weighing accurately 7.55g of PCT and dissolved in the 100ml of double distilled water taken in the beaker. The dopant EDTA is added in the concentration of 0.1M by weighing about 2.92g and mixed directly to PCT. These were filtered.

2.2. Crystallisation method

The beaker was covered with filter paper. Small holes were made on the filter paper. The solution was allowed to evaporate slowly. Crystals formed were harvested after few days.

RESULTS AND DISCUSSION

3.1 FTIR Analysis

The FTIR spectrum for pure as well as doped crystals were recorded using FT-IR instrument using the KBR pellet technique in the range 400-4000cm^{-1} which is shown in the Fig. 1 & 2. The calculated frequencies with their relative intensities obtained in FTIR of pure and doped paracetamol and their most probable assignments are presented in Table(1)

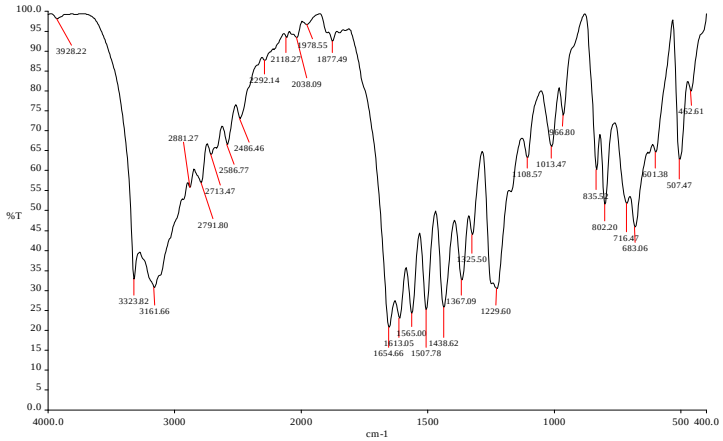

Fig.1 FTIR Spectrum of Pure PCT

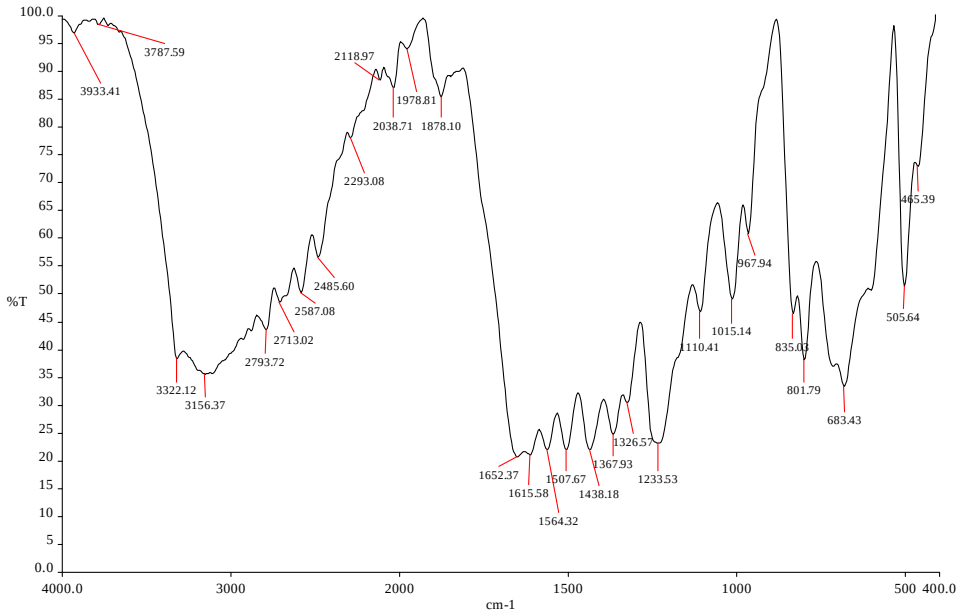

Fig. 2 FTIR Spectrum of EPCT

Table 1. IR Absorption Frequencies of Paracetamol and EPCT Crystals

Wave Number(cm^{-1})		Assignment
Paracetamol	EPCT	
3928.22	3933.41	O-H Stretching
-	3787.59	Intermolecular hydrogen bonded O-H stretching
3323.82	3322.12	N-H Stretching
3161.66	3156.37	N-H Stretching Associated, Intramolecular hydrogen bonded O-H Stretching
2881.27	2793.72	Symmetric C-H Stretching, Intramolecular hydrogen bonded O-H Stretching
2713.47	2713.02	Intramolecular hydrogen bonded O-H Stretching
2586.77	2587.08	
2486.46	2485.60	
2292.14	2293.08	
2118.27	2118.97	
2038.09	2038.71	C-H out-of-plane bending
1978.55	1978.81	
1877.49	1878.10	
1654.66	1652.37	C=O Stretching
1613.05	1615.58	Aromatic C=C Stretching
1565.00	1564.32	Aromatic C=C Stretching, N-H Deformation
1507.78	1507.67	Aromatic C=C Stretching, N-H Deformation
1438.62	1438.18	Asymmetric C-H bending
1367.09	1367.93	Symmetric C-H bending
1325.50	1326.57	C-N Stretching
1229.60	1233.53	C-O bond
1108.57	1110.41	
1013.47	1015.14	
966.80	967.94	Asymmetrical ring Stretching
835.52	835.03	Aromatic C-H out-of-plane bending
802.20	801.79	
716.47	-	OH-out-of-plane bending
683.06	683.43	Aromatic C-C out-of-plane bending
507.47	505.64	N-H out-of-plane bending

Considering the spectra of paracetamol and EPCT, the EDTA approaches the paracetomol lattice and occupies the interstitial spaces and form intermolecular hydrogen bonding with acetimido grouping and due to this, there is no much variation in all the assigned frequencies[12].

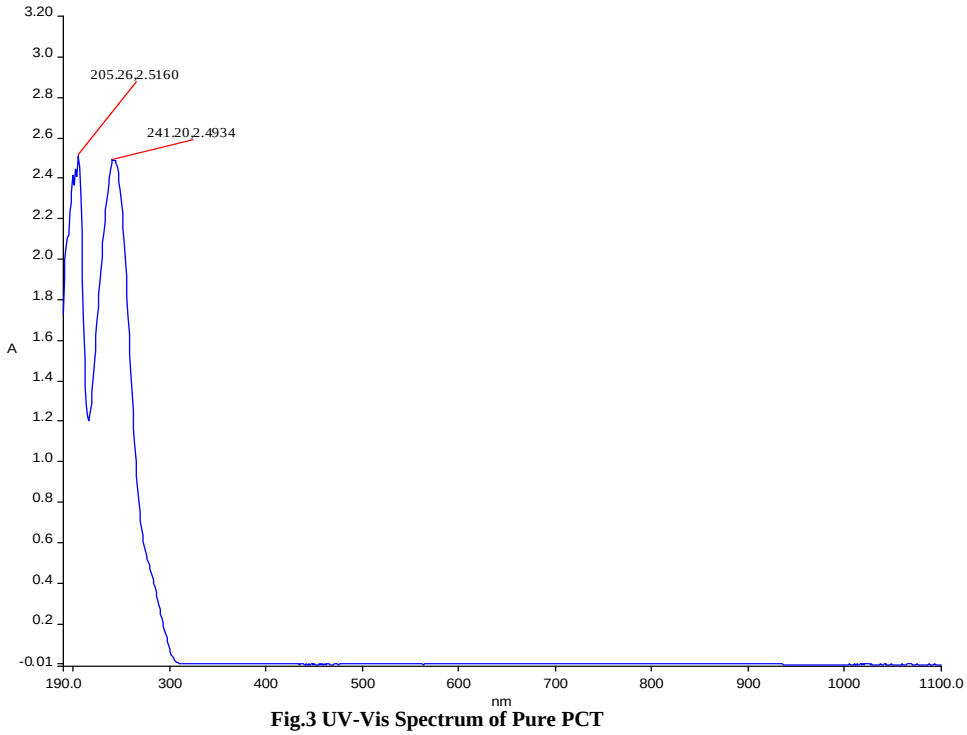

Fig.3 UV-Vis Spectrum of Pure PCT

3.2 UV Spectral Analysis

The UV-Visible spectral study is a useful tool to determine the transparency, which is an important requirement for material to be optically active. The UV-Visible spectrum of PCT and EPCT were recorded in the range of 190-

1100nm, using lambda spectrometer at a scan speed of 480.00nm/min. The UV-Visible spectra of paracetamol and doped paracetamol is shown in the Fig.3 and Fig.4.

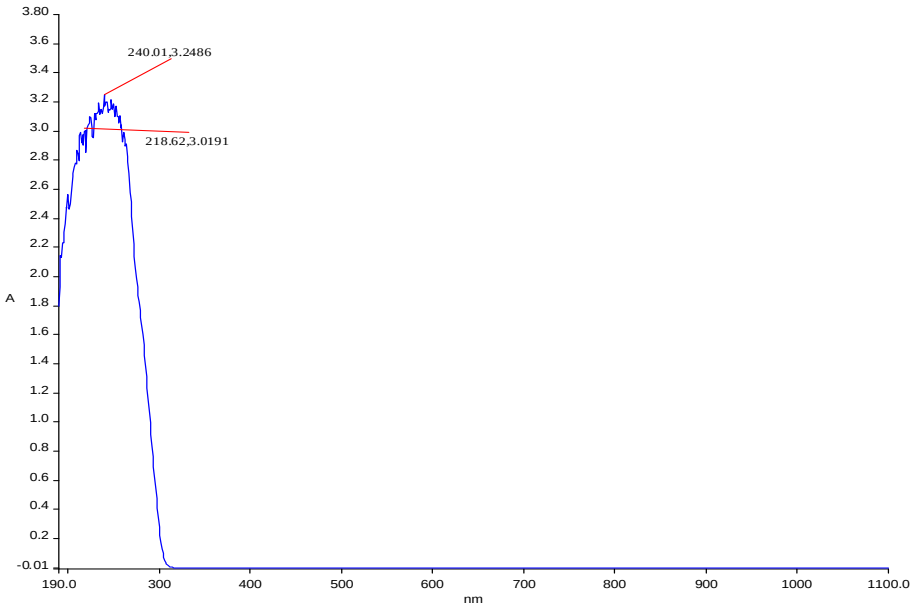

Fig.4 UV-Visible Spectrum of EPCT

As there is no considerable change in the cut-off wavelength, due to the addition of EDTA and hence for both UV and Visible region, the paracetamol and EPCT can be used as an optical window. Regarding the electronic absorption, the Bathochromic shift is observed in the imido carbonyl oxygen from 205.26nm to 218.62nm.

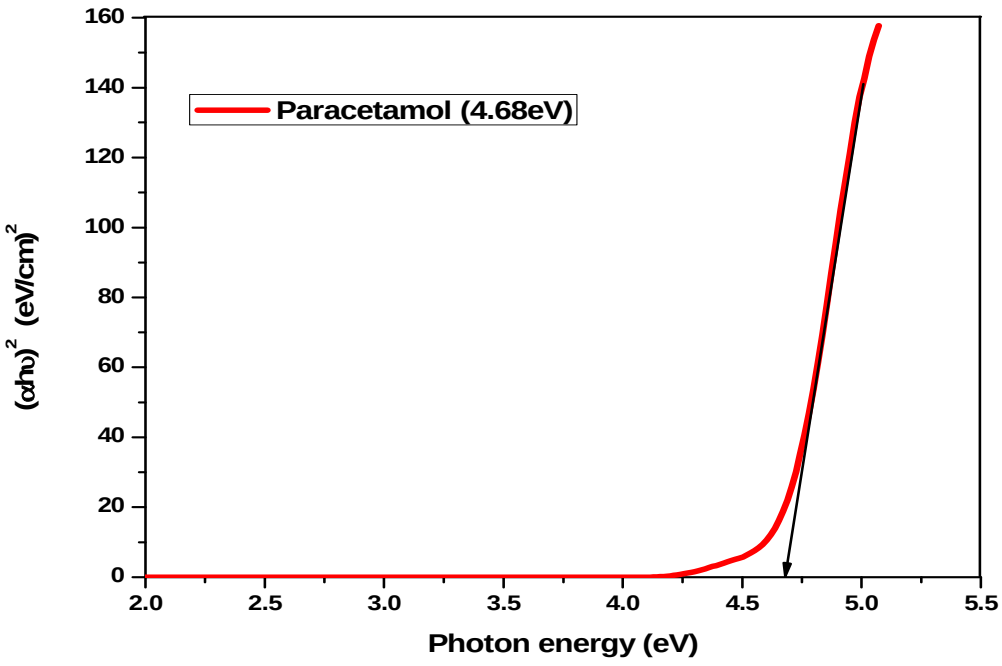

Fig.5 Band Gap Energy of Pure PCT

3.3 Band Gap Energy Determination

The band gap measurement was also carried out for PCT and EPCT crystals. The plot of $(\alpha h\nu)^2$ against hν is shown in the Fig.5 and Fig.6, a trend line was added to extrapolate and it cut the X-axis of 4.41eV which is taken as the direct band gap of the crystal.

Due to the addition of EDTA, the band gap values decreases from 4.68eV in pure paracetamol to 4.41eV in doped PCT which indicates that the laser activities decreased in EPCT and used as an optical window in visible region[9].

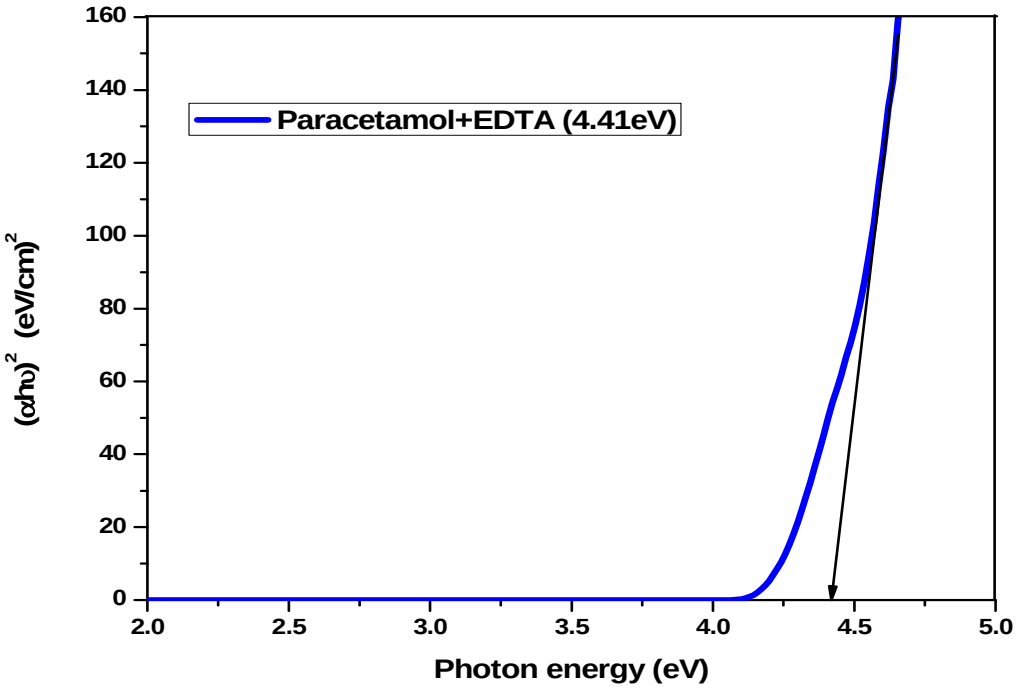

Fig.6 Band Gap Energy of EPCT

3.4 Thermal Analysis

The crystals of EPCT was subjected to thermogravimetric analysis, differential thermogravimetric analysis, using a Q500 V20.10 Build 36 thermal analyser in nitrogen atmosphere. The samples were heated between 30°c and 930°c to study the mass loss and thermal stability. The TG-DTG curves of grown crystals were shown in the Fig.7.

The thermogram illustrates the absence of weight loss up to 140 ^{0}C. Hence, the crystal is devoid of any physically adsorbed water molecule. There is a small weight loss of 1.75 % at 150°c. It is due to the liberation of hydrogen gas. The next major weight loss of 96.63% occurs between 150°c and 350°c shows that the decomposition is almost complete. Due to the addition of the dopant, in the DTA analysis, the sharp exotherms observed at 270 ^{0}C coincides with the weight loss in TGA Curve. This confirms the crystal is EPCT rather than pure paracetamol[10-11].

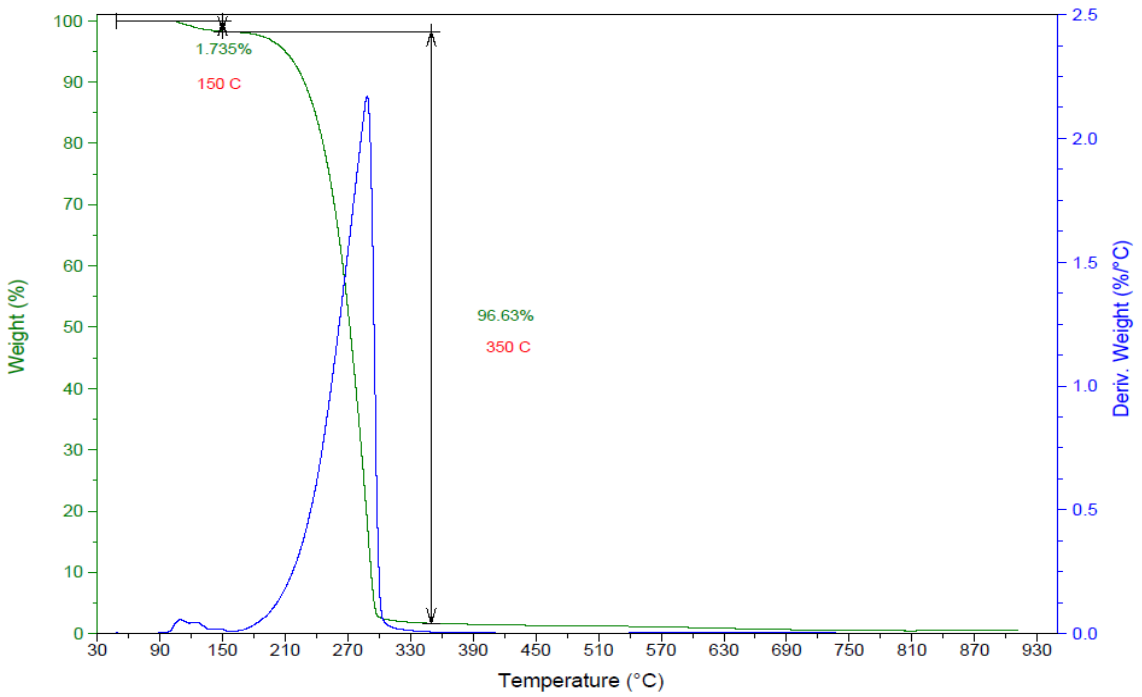

Fig.7 TG-DTG Curve of EPCT

3.5 Single Crystal X-ray Diffraction

The single crystal X-ray diffraction analysis on EDTA doped paracetamol single crystals was recorded using X-ray diffractometer. This analysis has revealed that the single crystals of doped paracetamol crystallize in monoclinic system. The unit cell dimensions for doped paracetamol are compared with that of pure paracetamol and are given in table(2). The XRD analysis revealed that the addition of dopant in the paracetamol does not change the crystal structure though there is a change in the cell dimensions

Table 2: Comparison of unit cell dimension

	Pure Paracetamol	Doped paracetamol
a(A°)	7.13	14.15
b(A°)	9.40	18.69
c(A°)	11.79°	12.88
α	90.00°	90.00°
β	97.19°	113.44°
ϒ	90.08°	90.00°
Volume	784A^{o3}	3076A^{o3}
System	monoclinic	monoclinic

3.6 Scanning Electron Microscopic Analysis

The image in SEM is produced by scanning the sample with a focused electron beam and detecting the secondary and back scattered electrons from the conventional SEM image. The SEM micrograph images of EPCT are shown in the Fig.8 and Fig. 9 respectively. The SEM image clearly reveals that due to the addition of complexing agent EDTA, the growth pattern is modified and also Nano Ellipsoidal structure like growth pattern on the surface of the grown crystal is observed.

3.7 Energy Dispersive X-ray Analysis

Fig.10 shows EDAX spectrum of EPCT crystals. The peaks show the presence of Carbon, Nitrogen and Oxygen in the Crystals. Table.3 shows the elemental and atomic percentage of the elements C,N and O. It was observed that the atomic % of C,N and O are 80.54, 2.55 and 16.91 respectively. The result shows that the atomic % of C increases and atomic % of N decreases due to the addition of dopant and also reveals the absence of any other impurities in the crystals.

3.8 Optical Image Microscope

The crystals are photographed using Optical Microscopy LX400. The EPCT crystals are colourless and transparent. The photographs of the crystals are shown in the Fig.11.

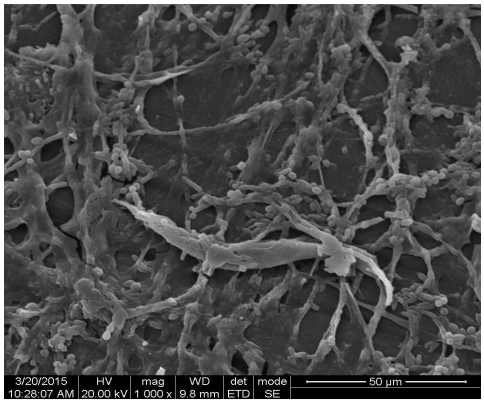

Fig.8 SEM image of EPCT

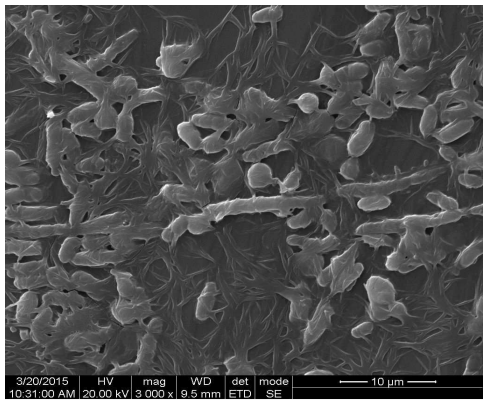

Fig.9Magnified SEM image of EPCT

Table.3 Elemental Data of EPCT

Element	***Wt%***	***At%***
CK	75.95	80.54
NK	02.80	02.55
OK	21.25	16.91
Matrix	Correction	ZAF

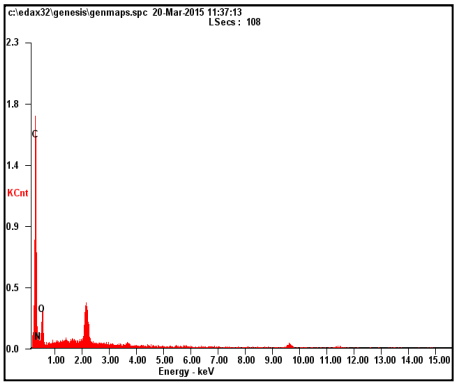

Fig.10 EDAX Spectrum of EPCT

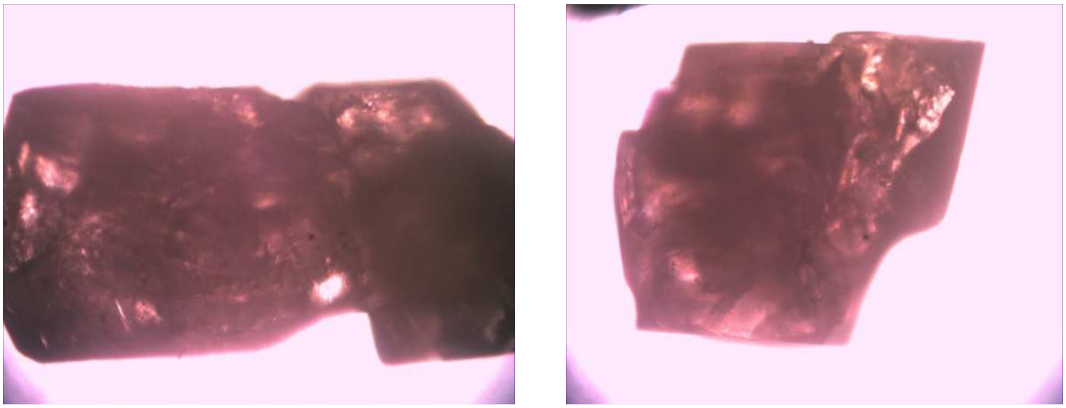

Fig.11 Optical Microscopic images of EPCT

CONCLUSION

In the UV absorption studies, it was observed that there is no change in the cut-off wavelength, the EPCT can be used as an optical window. It is also evident that due to the addition of compexing agent EDTA to paracetamol the band gap value decreases which confirms the decreasing laser activity property. It is also evident from FTIR studies that binding of EDTA with paracetamol from the frequency assignments. The Thermo gravimetric study confirms the decomposition pattern of EPCT. In SEM images a Nano ellipsoidal structure like growth is observed. Evaluation of Unit Cell dimensions and volume confirmed that the dopant EDTA has gone into the PCT crystal lattice.

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