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Growth and characterization of EDTA doped BupropionHydrochloride

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ABSTRACT: *Good transparent single crystals of EDTA doped BupropionHydrochloride are successfully grown by using slow evaporation technique at room temperature with double distilled water as solvent. The vibrational modes of the molecules are elucidated from FTIR spectra. Its optical behavior has been examined by uv-vis spectral analysis, which shows the absence of absorbance in the visible region. Thermal properties of EDTA doped BPH crystal were carried out by TGA and DTA technique which indicate the thermal stability of the sample. The effect of the influence of dopant on the surface morphology of EBPH crystal faces are analyzed by Scanning Electron Microscope (SEM). The energy dispersive X-ray analysis(EDAX) of EBPH show the almost same composition. The grown crystals were subjected to powder X – ray diffraction studies to identify the morphology and structure.*
Keywords*: crystal growth, X –ray diffraction, optical absorption studies, Thermo gravimetric analysis.*

I. INTRODUCTION

In the last years, many leading pharmaceutical companies have begun to strictly control the crystal chemistry of active pharmaceutical ingredients during their preparation and development stages (1). But in the recent past, crystal polymorphism has pervaded the field of solid state organic chemistry and particularly, drug development and formulation, from basic science to industrial process control, up to patent litigation and infringing issues. The reason for such a blooming comes from the well – established knowledge that different polymorphs can have markedly different physico – chemical properties. (2) Bupropion hydrochloride is a white crystalline powder. It belongs to the chemical class of aminoketones and it is known also with generic name of amfebutamone hydrochloride. It is a second generation antidepressant. It is used as a selective inhibitor of dopamine uptake. It inhibits neuronal nicotinic acetylcholine receptors (3) BPH is one of two non- nicotine based medications used to help quit smoking (4). The dopant EDTA is also known as artificial amino acid and it is a hexadentate ligand. The effect of impurities on growth rates and morphology has been discussed in many articles (5 – 8). As no reports are available on the growth and characterization of EDTA doped BPH crystals. In this work, we report on the growth and characterization of EDTA doped BPH crystals by slow evaporation technique. Here after, the grown crystals are named as EBPH (EDTA doped Bupropion hydrochloride)

II. EXPERIMENTAL

Pure BPH was purified by successive recrystallisation. The crystals were grown by a slow evaporation solution growth technique. A saturated aqueous solution of BPH was prepared. EDTA was taken as dopant with the 0.1 mol concentration and added to the BPH solution.The solution was filtered. The seed crystals are allowed to float on the surface of the saturated solution and left for slow evaporation at room temperature. The crystallisation took place within three weeks and the optically transparent crystals were obtained.

III. RESULT AND DISCUSSION

FTIR Analysis: The FTIR spectra for pure as well as doped BPH crystal were recorded, using FTIR instrument, using the KBr pellet technique in the range 400 – 4000 cm^{-1}. The calculated frequencies are agreed with the observed frequencies. The frequencies with their intensities are obtained in FTIR of pure and doped BPH and their most probable assignments are presented in Table 1. As EDTA is a very good complexing agent, it occupies the interstitial position in between the N-C bond of BPH and as a results there is a considerable shift is observed in the asymmetric N-H bond stretching secondary amine peak and also aromatic C-H stretching frequency and correspondingly the N-C stretching, C = O stretching and symmetric N-C bending frequencies are absent may be due to the steric strain of the interstitial occupancy of EDTA in the lattice of BPH. Because of this also, there is considerable shift in the asymmetric C-H bending and C-C bending frequencies.(9).The FTIR spectrum of EDTA doped BPH, and pure BPH are shown in the Figure 1,2 respectively.

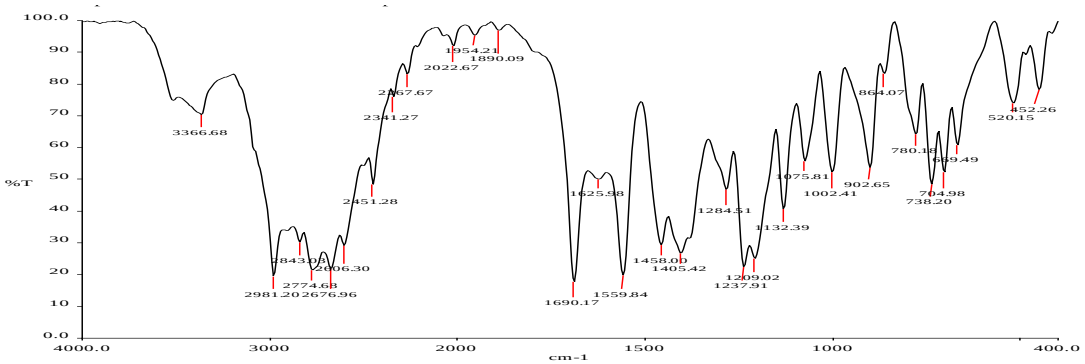

Figure 1 FTIR spectrum of EBPH

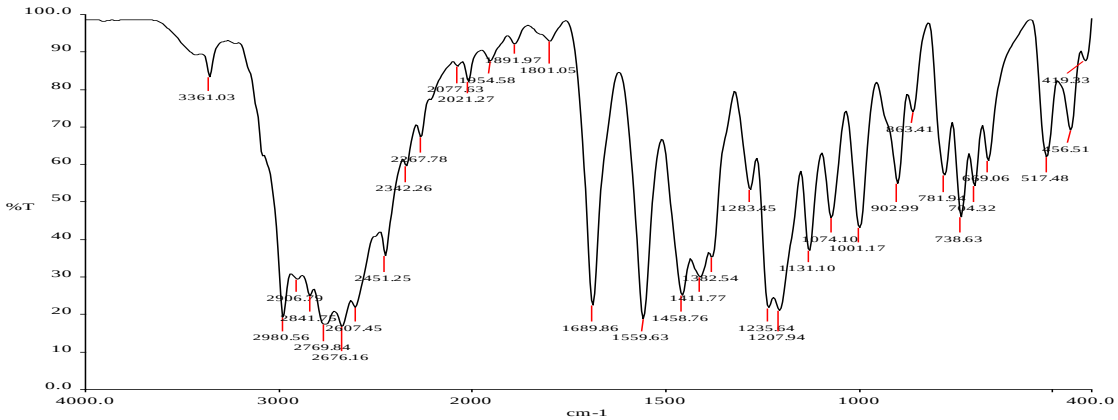

Figure 2 FTIR spectrum of pure BPH

BPH	EBPH	Frequency Assignment
3361.03	3366.68	Asymmetric NH Stretching secondary amine one peak
2980.56	2981.20	Aliphatic C-H stretching (4 CH_3 group)
2906.79	-	Aliphatic C-H stretching
2841.75	2843.03	Aliphatic C-H stretching (two (or) three bands)
2769.84	2774.68	Aromatic C-H stretching
2676.16	2676.96	NH stretching vibration group of relative sharp bands due to overtone and combination band (or) overtone and combination band of OH plane bending
2607.45	2606.30	
2451.25	2451.28	
2342.26	2341.27	
2267.78	2267.67	
2077.63	-	N-C stretching
2021.27	2022.67	N-C stretching
1954.58	1954.21	Overtone peak band
1891.97	1890.09	Weak combination band
1801.05	-	C=O stretching
1689.86	1690.17	C=O stretching
-	1625.98	Skeletal vibration of benzene ring
1559.63	1559.84	Aromatic C=C stretching
1458.76	1458.00	N-H bending
1411.77	1405.42	Asymmetric C-H bending (or) OH in plane bending
1382.54	-	Symmetric C-H bending (or) N-C bending
1283.45	1284.51	N-C bending
1235.64	1237.91	C=O bending
1207.94	1209.02	C=O bending
1131.10	1132.39	Asymmetric C-N-C stretching
1074.10	1075.81	Aromatic C-Cl stretching
100.17	1002.41	In plane C-H bending
902.99	902.65	O-H out of plane bending
863.43	864.07	C-H out of plane bending
781.94	780.18	m– disubstituted benzene ring
738.63	738.20	N-H out of plane bending
704.32	704.98	m – disubstituted benzene ring
669.06	669.49	C-H bending
456.51	452.26	C-C bending

Table 1-Vibrational frequency obtained for pure BPH and EBPH crystals

UV–VIS NIR Spectral Analysis : The UV – VIS – NIR absorption spectrum of the grown crystal was recorded on the wavelength range of 190 and 1100 nm using lamda 35 UV – VIS – NIR spectrophotometer in order to determine the transmission range and hence, the suitability of the crystals for optical applications. The recorded UV – VIS – NIR absorption spectrum of the pure BPH and EBPH is shown in the Figure 3and 4. From the spectrum, it is noted that the cut off wavelength region increases due to the addition of the complexing agent EDTA as dopant. The UV visible absorption bands of BPH and EDTA doped BPH has got the following λ max along with the corresponding transitions are given below in the Table 2

compound	chromophore	λ max	Transitions
BPH	C=0	296.98	$n-\pi^*$
	N-H	222.95	$\pi-\pi^*$
EDTA doped BPH	C=0	296.79	$n-\pi^*$
	N-H	226.21	$\pi-\pi^*$

Table 2 Observed Transistions in BPH and EPBH

The corresponding n-π^* of the ketone group is not very much shifted due to the addition of the dopant, but the same time the absorption frequency corresponding to imide linkage is very much shifted to higher frequency region which supports the interstitial occupancy of EDTA closer to imide bond in BPH and hence, steric strain is enhanced and felt in the absorption spectra which affects the electronic environment and affect the electronic absorption in that region. (10,11).

The optical band gap of the BPH crystal and EBPH crystal was determined from the absorption spectrum using the near – band edge absorption relation

$(\alpha h v)^n = A (h v - E_g)$

Where A - the optical transition dependent constant, Eg – optical energy band gap, v - the frequency of the incident beam, A – Planck's constant n – characterizes the transition. Figure (0 shows the plot of $(\alpha h v)^2$ against h v . The intercept of the straight line on the photon energy axis given the direct band gap value of 3.72 ev for EBPH and 3.90ev for EPBH

The band gap energy BPH crystal and EBPH crystal are shown in the figure(5)

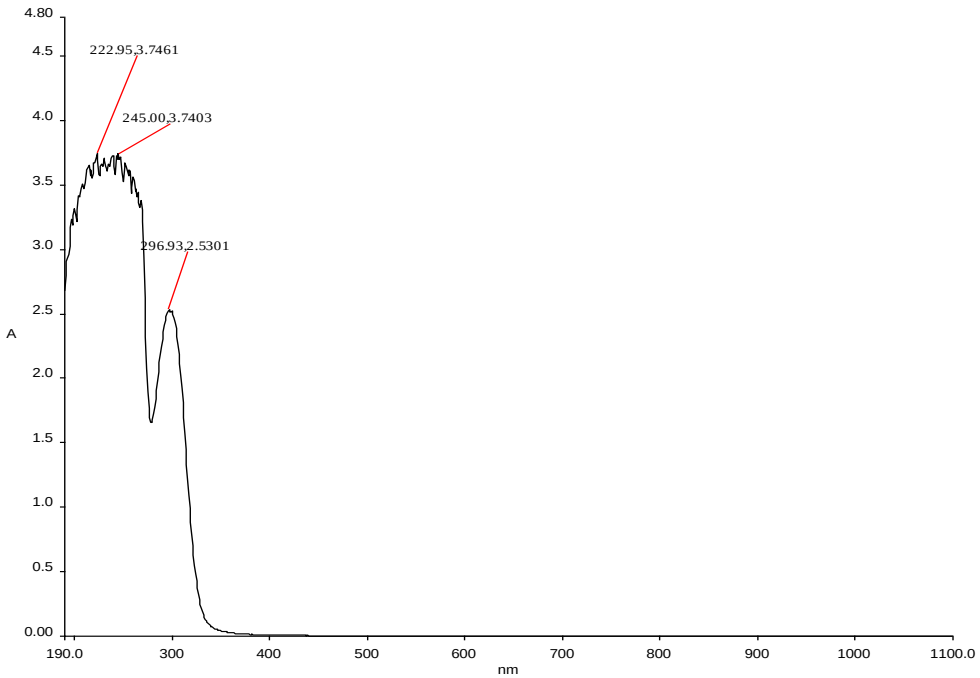

Fig 3: UV- Vis absorption spectrum of BPH

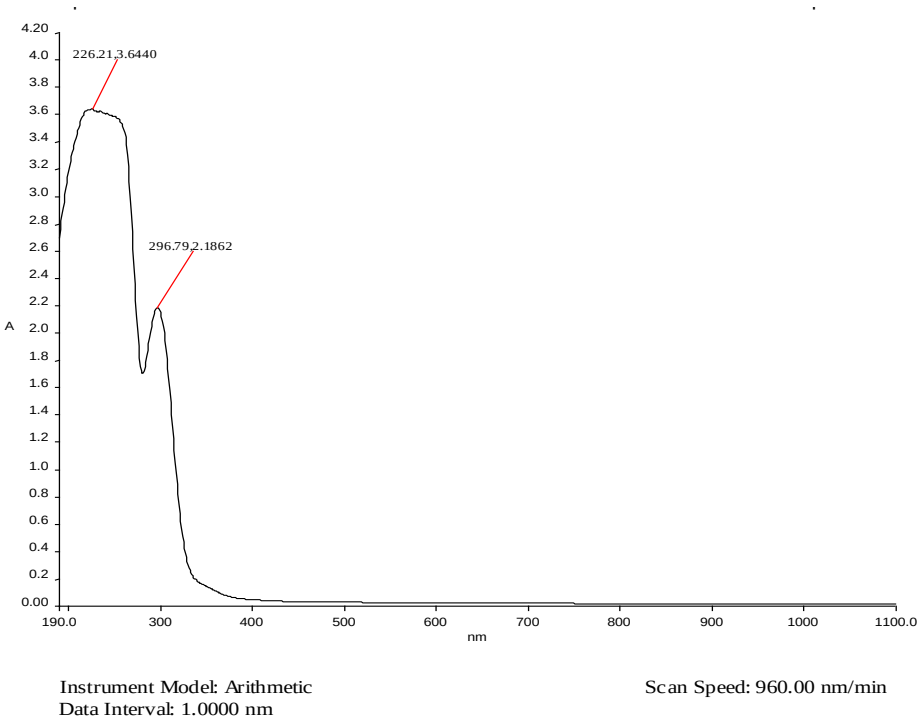

Fig 4: UV- Vis absorption spectrum of EBPH

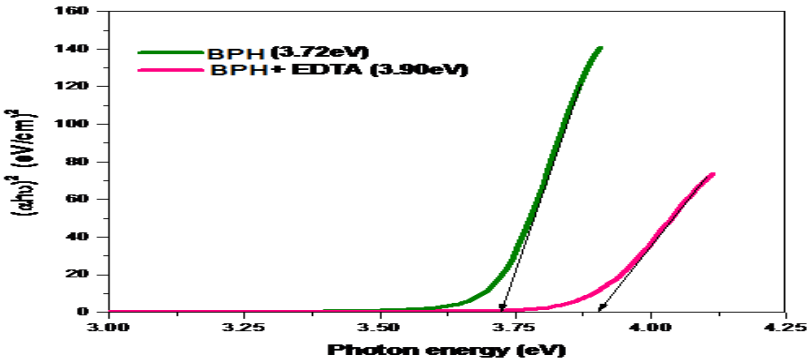

Figure 5 Band gap energy of BPH and EBPH

Thermal Analysis : Thermo gravimetric analysis (TGA),Differential thermal analysis(DTA) were carried out ,using TGA Q500 V_{20} 10 instrument, recorded in the same chart are shown in the figure(6).Thermo gravimetric analysis (TGA) is a technique in which the weight of a substance is recorded as a function of temperature. In the present case, the TGA and DTA are carried out between 30^0 C and 930^0 C in the nitrogen atmosphere which provide an inert environment. The thermogravimetic results are governed by the weight and particle size. In practice, a small sample weight is desirable for thermo gravimetric results (11).

In figure (6) there are three distinct weight losses above 120^0 C. At the first stage, about 63.94% of weight loss at 300^0C which is assigned to the loss of Dimethylenediamine diacetic acid, chlorobenzene and Co_2. At the second stage at 550^oC, ther is one more weight loss of 14.68% due to the loss of acetaldehyde and Co_2. In the final step, due to the loss of trimethylamine and hydrochloride there is 19.38% of sample violated, leaving about 2.10% of the sample as end residue at 910^oC. However, in the DTA curve an exothermic peak which is not much sharp may be assigned to melting point of the BPH. The other exotherms nearly Coincide with the TGA weight loss prediction.

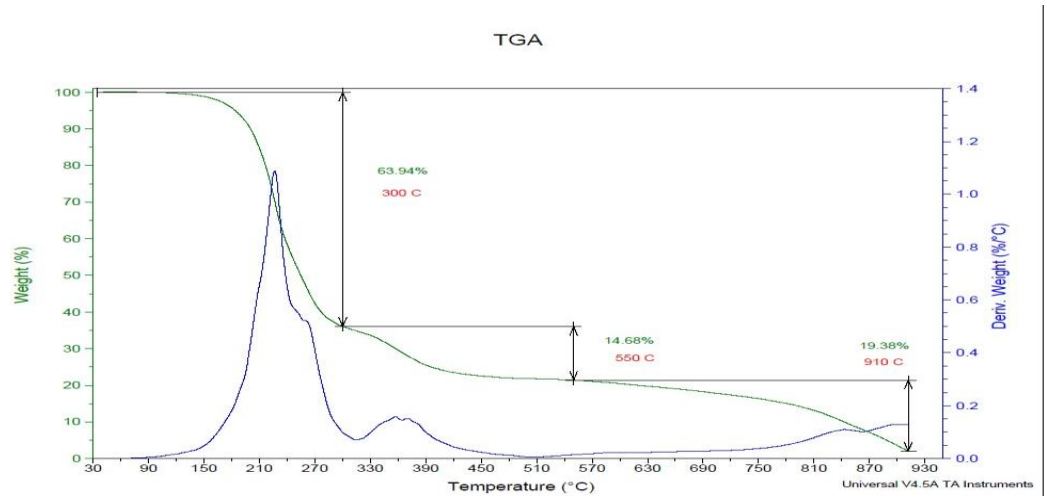

Figure 6 Recorded TGA-DTA of EBPH

3.2 Powder X – ray diffraction analysis

The crystallinity nature of the obtained sample was identified by powder X - Ray difractometer. The sharp intensity peak shows the measure of crystalline nature of the compound. The XRD patterns for EDTA doped BPH are shown in the figure (7). The single crystal XRD determination by BPH is found to be monoclinic system with p21/c space group and the corresponding unit cell dimension are a = 14.3250(8) A,b = 8.7453(4) A, c = 11.8646(7)A and the corresponding angle are $\alpha = 90^0$, $\beta = 101.959^0$ (2), $\gamma = 90^0$ and the cell volume is found to be 1454.09 (14) 4^3 and the dopant EDTA was incorporated into the BPH structure which can be identified by taking the X-ray - powder diffraction data of mixed crystal . it is found to be the 2Ø values & d values corresponding to EDTA (JCPDS cd No. 33 – 1672) is observed in the powder diffraction data of the mixed crystal which shows the EDTA has entered into the crystal BPH.

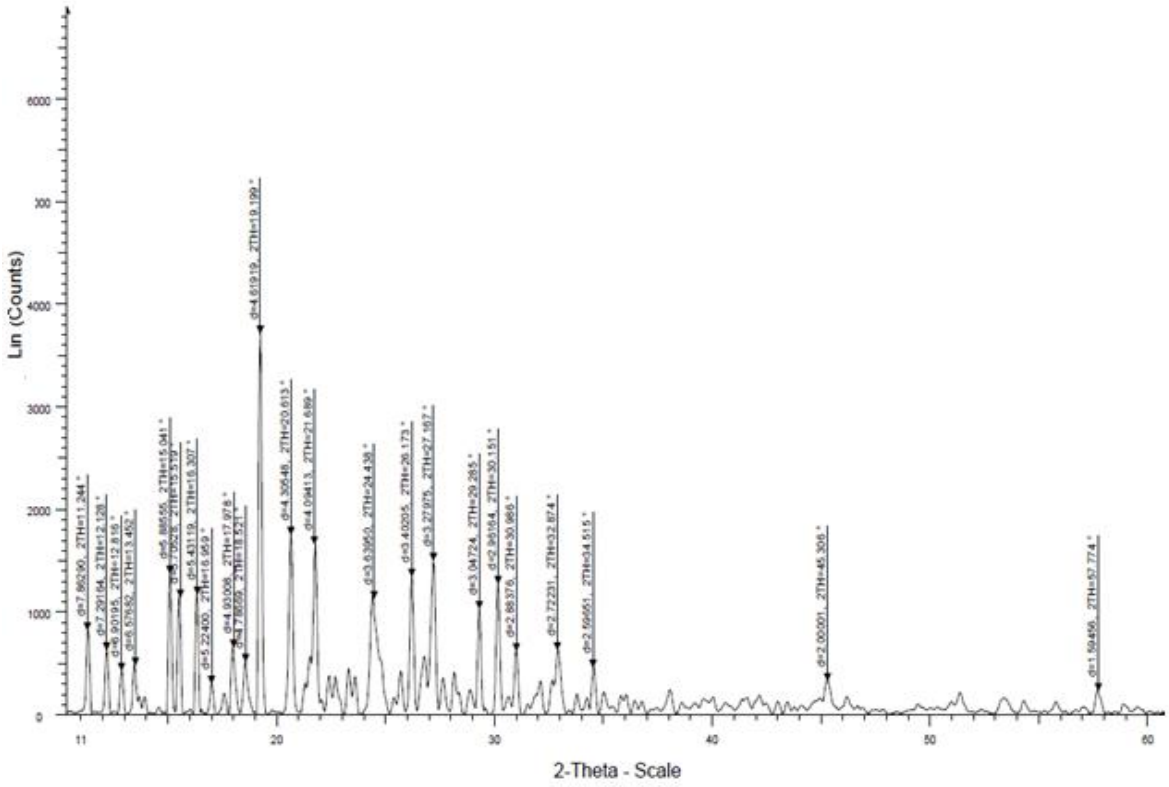

Figure 7 Powder XRD pattern of EBPH

Scanning Electron Microscope Analysis: Scanning the surface with a high energy beam of electron in a raster scan pattern is call ed Electron Micrescope. The shape and size of the particles making up the object can be viewed and studied. Figures (8 a,b,c,d) show the SEM image of the as grown BPH and EDTA doped BPH. In case of the different magnification picture shows that there is stepwise parallel type of layer growth is observed on the surface but due to the addition of the dopant EDTA, the growth pattern is modified and also vertical and crosssectional layer growth is observed and hence EDTA acts as a excellent growth modifier in the biocrystals which can be very much useful for its applications.

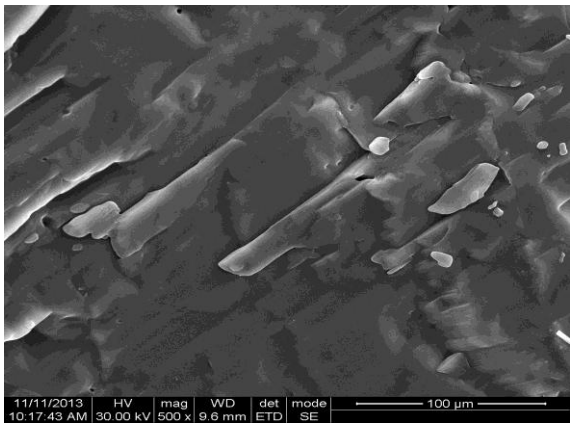

Figure 8 (a) SEM image of BPH

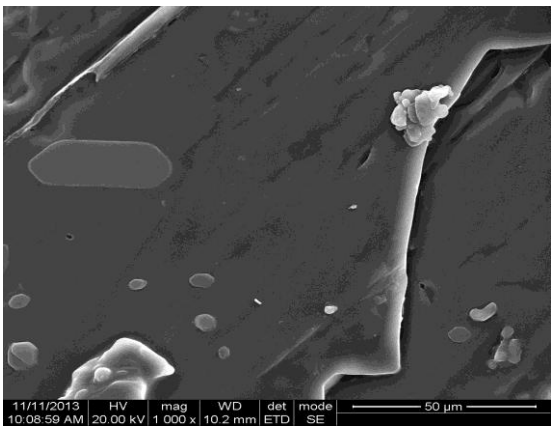

Figure 8 (b) Magnified SEM image of BPH

Figure 8 (c) SEM image of EBPH

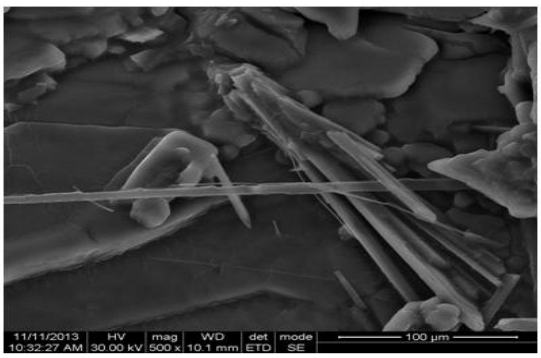

Figure 8 (d) Magnified SEM image of EBPH

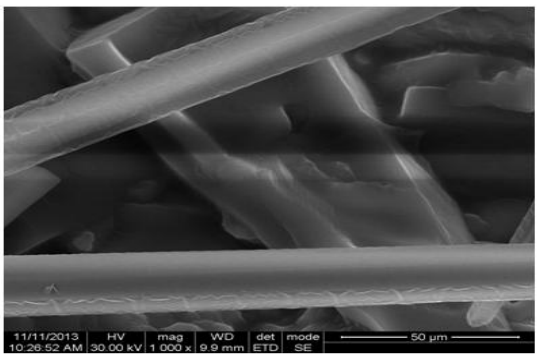

Figure 8 (c) SEM image of EBPH

Figure 8 (d) Magnified SEM image of EBPH

Energy Dispersive X – ray Spectroscopy (EDAX) : Figure (9) shows EDAX spectrum of EDTA doped BPH crystal. The peaks show the persence of Oxygen, Nitrogen, Carbon and chlorine in the crystals. Table 3 shows the elemental and atomic percentage of the elements C,O,N and Cl. It was observed that the atomic % of C,N,O and Cl are in good agreement with stoichiometrically expected atomic % 77.34,6.29,4.27,11.76 respectively (14).

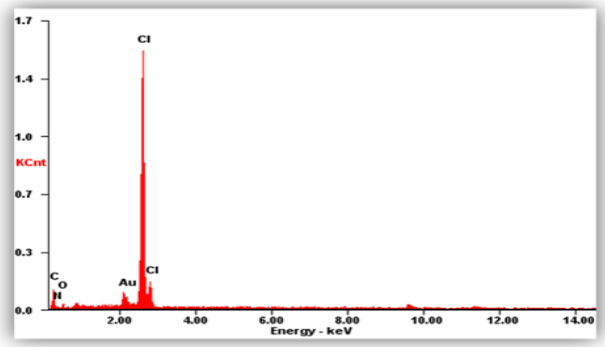

Figure 9 EDAX spectrum of EBPH

Element	Wt%	At%
CK	59.22	77.34
NK	05.61	06.29
OK	04.36	04.27
AuM	04.23	00.34
ClK	26.58	11.76
Matrix	Correction	ZAF

Table 3. Elemental Composition of EBPH

IV. CONCLUSIONS

Good optical quality EDTA doped BPH crystals were grown using water as the solvent. The slow evaporation of the solvent yielded good quality crystals. The lattice parameter values and the crystalline nature of grown crystal had been confirmed by powder XRD.Thermal analysis revealed that the grown crystals are thermally stable up to 120^{o} c. From UV – Vis spectra of grown crystals, it is confirmed that the crystals have excellent optical quality. From FT – IR spectral investigations, molecular structures of pure and doped samples are verified. Changes in intensity of peaks for doped samples compared to pure BPH are due to interaction between parent and dopant. It is concluded that EDTA are well incorporated into the BPH crystal. The SEM studies suggested vertical and cross sectional layer growth.EDAX studies reveals that grown crystals are EBPH indeed.

REFERENCES

[1]. R.Hilfiker,Polymorphism in the Pharmaceutical Industry, Wiley – VCH,2006
[2]. R.Hilfiker, F-Blatter,M.Von Raumer,in : Rof Hilfker (Ed), Relevance of Solid – state properties for pharmaceutical products in polymorphism in the Pharmaceutical Industry, Wiley – VCH Verlag GmbH & Co. KgaA.2006.
[3]. J.Etourneau .Bull. Mater. Sci. 22,165 (1999) 2009; 71; 1634 – 1637
[4]. Gold Stein MG. Bupropion sustained release and smoking cessation. J.Clin Psychiatry – 1998; 59 Suppt 4:66- 72
[5]. Chandrasekaran J,Illayabarathi P,Maadeswaran P,Mohamed Kutty P,Pari S, Synthesis, growth and characterization of a semiorganic nonlinear optical single crystal: L – Valine cadmium bromide – optik.2012; 123:1407 – 1409
[6]. Jeffery GH, Bassett J, Mendham J, Denney RC, Vogul's text book og Quantitative Chemical analysis (ELIBS). Addison Wesley Longman Limited. UK;1989.
[7]. Meera K, Claude A, Muralidharan R, Choi CK, Ramasamy P. Growth and characterization of EDTA – added TGS crystals. J.crystal Growth. 2005 ; 285 : 358 – 364.
[8]. Lawrence M, Thomas Joseph Prakash. Growth and characterisation of pure and glycine doped cadmium thiourea sulphate (GCTS) crystals. Spectrochemica Acta part A. 2012 ; 91 : 30 – 34.
[9]. Y.R. Sharma, Elementary Organic Spectroscopy , Principles and Chemical Applications, First Edition 72 – 133 (1980).
[10]. Sankar R, Raghavan Cm, Balaji M, Mohankumar R, Jeyavel. Synthesis and Growth of Triaquaglycine sulfatozinc (11), a new semiorganic Nonlinear optical crystal. R. crystal. Growth & Design. 2007 ; 7 ; 348 – 355.
[11]. Vijayan N,Ramesh Babu R, Gunasekaran M, Gopalakrishnan R, Ramasamy P, Kumaresan R, Lan CW. Studies on the growth and characterisation of P- hydroxy acetophenone single crystals. J.Cryst. Growth. 2003; 249: 309 – 315 .
[12]. Gopalan. R, etal, Elements of Analytical Chemistry. Second Edition, 171 – 183, 199 – 216 (1994).
[13]. Anie Roshan S, Cyriac Jaseph, Ittyachen MA. Growth and characterisation of a new metal – organic crystal ; potassium thiourea bromide.Mat. Lett. 2001 ; 49 : 299 – 304.
[14]. H.M.Pattil,D.K.Sawant,D.S.Bhavsar, J.H.Patil and K.D. Girase. J. Therm. Anal.Chem., 2001. DOI 10.1007/s 10973 – 011- 1599 – 1.