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Determination of the characters of carbamazepine using three different alternative techniques, Fourier Transform Infrared, Differential Scanning Calorimeter, and Scanning Electron Microscope

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ABSTRACT

There are many different analytical techniques used in pharmaceutical industry and pharmaceutical analysis such as Fourier Transformation Infrared Spectrometry (FTIR), Differential Scanning Calorimeter (DSC), and Scanning Electron Microscope (SEM).These techniques are useful in both qualitatively and quantitatively analysis. The current study used the three techniques (FTIR, DSC and SEM) to analyse carbamazepine (CBZ) sample to compare between them in order to ensure ideal chosen efficient technique. A CBZ sample was analysed by t FTIR. Another sample was recorded on DSC within about 10 min. In addition, the sample picture was taken by SEM within about 20 min.The results of FTIR, DSC and SEM techniques showed that the CBZ sample has functional groups such as alkenes and aromatic rings. Melting point (191.88 C°) with sharp peak with endothermic transformation (solid – solid) with enthalpy 95,5217 J/g and entropy 4,975 J/K. Furthermore, prismatic morphology with different particle size of CBZ and coarse texture. Depending on results of TIR, DSC and SEM techniques, it can be seen that three techniques are powerful tools due to give better understanding of physicochemical properties of CBZ when used with each other.

Key words: Fourier Transform Infrared, Differential Scanning Calorimeter, Scanning Electron Microscope, carbamazepine.

INTRODUCTION

Analytical techniques are instruments that are used to identify the composition of compounds in purpose of determining the amount of compound. However, the most analytical techniques have different methods in analysis e.g., FTIR, DSC, and SEM. To begin with FTIR spectroscopy, according to Smith [2] FTIR technique is an effective method, in which the spectra produced by passing infrared radiation through a sample. This spectrum provides information about a sample and produce a molecular fingerprint for sample that can be used to screen the elements of the sample and to measure the amount of material in it. It is widely applied technique for quantitative and qualitative analysis especially in pharmaceutical industry because it is suitable for analysis of various pharmaceutical forms such as solid and liquid [4]. Furthermore, it is used for monitoring the process of drug manufacturing, detection polymorphs of drugs and fingerprint test for films and coating during drug production. Moreover, it is reliable, economic technique and offers non-destructive chemical compositional analysis. Whereas, there is difficulty in interpretation of results of FTIR spectra due to overlapping bands and it has non accurate measurements for wavenumber and transmittance.

Secondly, DSC technique is a thermoanalytical tool which is used to measure the change of the difference in heat flow to a sample and a reference at an identical temperature which is registered as function of temperature [5]. DSC technique offers both qualitative and quantitative analysis by measuring endothermic (heat absorption) and exothermic (heat evolution) changes, which involved melting points and glass transition and these material's attribute used to identify the purity and identity of a drug substance. As well as, it is a useful technique in pharmaceutical and polymer industries because it provides the wide temperature operational range., In addition, it is a rapid technique and sample preparation is easy. However, DSC is unsuitable for analysis blend of various components due to overlapping results and the interpretation of results is complicated.

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Thirdly, SEM is a powerful magnification instrument which offers high-resolution imaging and three-dimensional images for surface specimen in order to obtain information about composition and topography of material surface [1]. The SEM is one of the most useful tools to provide information about the microstructure of pharmaceutical materials which is involved particle size, API characterization and contaminant identification. Also, it contributes in pharmaceutical development and production by supplying elemental analysis and high resolution imaging. Although expensive, it is very sensitive for vibrations and magnetic fields. However, sample preparation is also difficult.

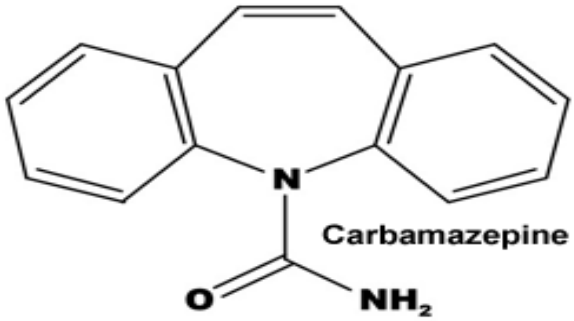

Fig.1 Structure of Carbamazepine (CBZ).

CBZ is an anticonvulsant drug and specific analgesic for trigeminal neuralgia with psychotropic properties., It is taken as chewable tablets of 100 mg, tablets of 200 mg, and suspension for treatment of epilepsy and trigeminal neuralgia [3]. It exists in multiple crystal forms (polymorphs). In addition, it has white to yellowish-white colour, odourless and no taste with melting point of 190 to 193°C. It is partially insoluble in water while soluble in alcohol, chloroform. It has to be noted that CBZ is insoluble in aqueous solutions, thereby indicating its behaviour as a "neutral lipophilic" substances which lead to limited dissolution rate as well as very slow absorption in gastrointestinal [7]. In addition, CBZ transforms from anhydrous to dihydrate form when exposed to moisture that lead to lose its activity and low bioavailability [8]. the chemical name of CBZ is 5H-Dibenz [b,f]azepine-5-carboxamide with trade names Tegretol and Biston. The molecular formula is C15H12N2O and molecular weight is 236.26.

There are various analytical techniques used to analyse CBZ, which play an important roles in assessing the quality of the drug by analysing physicochemical properties which can critically influence on quality of API. The aim of this work was to reveal effective technique from the three techniques (Fourier Transformation Infrared Spectrometry, Differential Scanning Calorimeter and Scanning Electron Microscope) in characterisation of the carbamazepine (CBZ).

METHODS

CARBAMAZEPINE

Carbamazepine (C15H12N2O) was powder, it supplied by Alfa Aesar Johnson Matthey Company (Lancs, UK).

FTIR

The FTIR spectrum of the carbamazepine (CBZ) sample was recorded over the region on 4000 - 450cm^{-1} using the diffusion reflectance IR Fourier Transformation of FTIR (Hamilton Sundstrand, Pomona, CA, USA) in the wavelength region 200-4000 nm.

DSC

The heat of fusion and melting behaviour of the sample were determined by a Mettler Toledo DSC 822e (Greifensee, Switzerland) at temperature rate between 50-250 C° with about 0.00528g of carbamazepine within about 10 min.

SEM

The SEM was used to study texture and particle size of (CBZ). The CBZ sample was fixed to aluminium stubs, and metallic coated and pictures of the sample were taken at 20 min, then and image analysis done using software package.

RESULTS AND DISCUSSION

The FTIR spectrum of the carbamazepine is depicted in (figure 2). In this experiment, the band characteristic of carbamazepine (CBZ) was found at 3464 cm^{-1} (NH-stretching of amine NH2), 1674cm^{-1} (- C=C- stretching of alkenes) and 1539cm^{-1}, 1388 cm^{-1} and 1254 cm^{-1} (C-C stretching in aromatic ring, C-H methyl rock with broad peak and C-N stretching). The band at 624cm^{-1} –C (triple bond) C-H is strong.

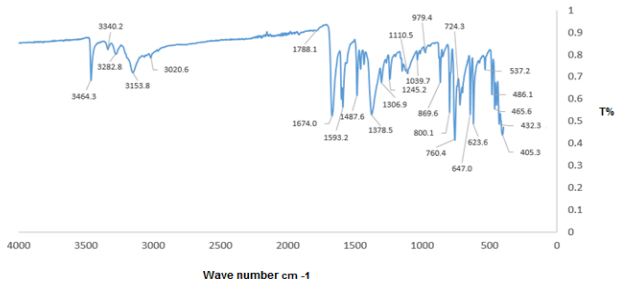

Fig.2 FTIR spectrum of Carbamazepine (CBZ).

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In the same way, the polymorph of carbamazepine (polymorph I) which was analysed directly by the diffusion reflectance IR Fourier Transformation. Figure (3) shows the FTIR spectrum of polymorph (ICBZ) [6], this spectrum is different from carbamazepine (CBZ) spectrum in both intensity and band position. There is a change of band position in higher wavenumbers. The band positions of polymorph (ICBZ) at 3484, 1684, 1397 cm^{-1} whereas the position band of carbamazepine (CBZ) at 3464, 1674 and 1379cm^{-1}. The intensity of (ICBZ) at 1254 cm^{-1}band was higher than 1270 cm^{-1}band in carbamazepine (CBZ).

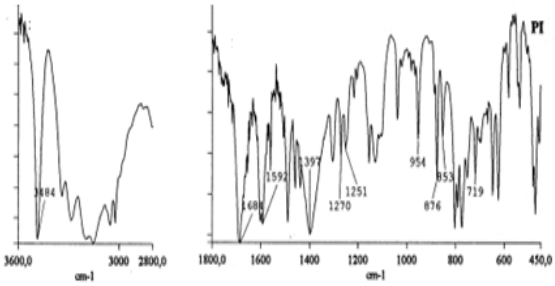

Fig.3 FTIR spectrum of polymorph (I CBZ) [6].

Characterization of Carbamazepine using DSC

In the carbamazepine (CBZ) experiment the sample was recorded on DSC at heating rate between 50- 250 C°. figure (4) shows two endothermic of fusion. The first peak with melting point was163.36C° due to loss of hydration, and the second sharp peak was observed indicating that the melting point of crystal structure was at191.88C°.

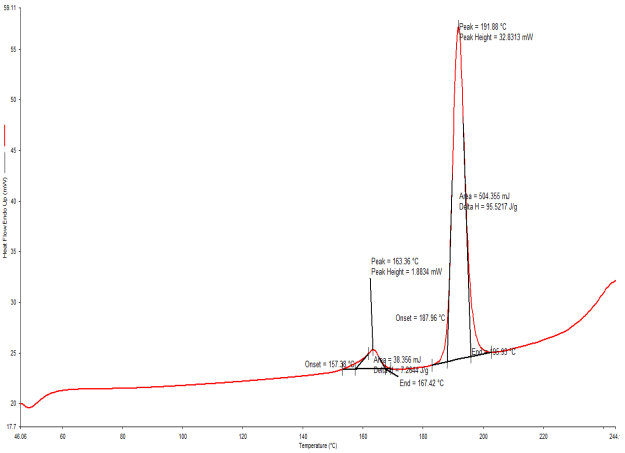

Fig.4 DSC profile of carbamazepine (CBZ).

On the other hand, P-Monoclinic (a polymorph of carbamazepine) is carried out on Perkin-Elmer DSC7 at heat range of 30 - 210 C° with 2-3mg weight. Fgure (5) reveals DSC curve of the P-Monoclinic [6]. As it can be seen, DSC curve of P-Monoclinic differed from carbamazepine (CBZ) showing two endotherms and one exothermic with larger enthalpy value. The first endothermic peak is at 178.8 C° followed by exothermic crystallisation and which subsequently melted at the second endothermic peak 193.2C°, which indicates the presence of an endothermal solid –solid transition. From the differences in results between two curves it can be seen clearly the impact of heat rate and material attributes of API on the shape of curves. Analytical temperature range significantly influences on melting point and DSC traces that lead to different curves and different transformation in polymorphs of carbamazepine [5].

Table1. It reveals the data of Carbamazepine experiments using DSC.

Experiment	Sample	Wt (g)	Temp. rate	Melting temp(Tm)	Tonset	Tendest	Enthalpy of melting (ΔH)	Entropy of melting (ΔS)
(CBZ) experiment	Carbamazepine	0.00528g	50 -250C°	First Peak 163.36 C° Second peak 191.88 C°	Frist peak 157.38 C° Second peak 187.96 C°	Frist peak 167.42 C° Second peak 195.93 C°	Frist peak 7.2644 J/g Second peak 95.5217 J/g	Frist peak 446 J/K second peak 4,975 J/g
P-Monoclinic (Literature Experiment)	P-Monoclinic (polymorph of carbamazepine)	0.002 – 0.003g	30 - 210C°	first Peak 174.8 C° Second peak 193.2C°	/	/	Second Peak 6.41Kcal/mol or 26,819.44 J/g	Second Peak 1,238.412Kcal /mol or 5,181,515.81 J/g

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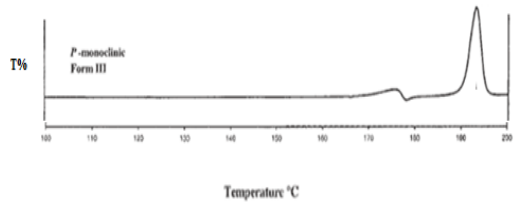

Fig.5 DSC curve of P-Monoclinic (a polymorph of carbamazepine) [6.]

Characterization of Carbamazepine using SEM The below figure (6a) shows the electron micrograph of carbamazepine (CBZ). As can be seen prismatic morphology and large particles of carbamazepine with rough texture and specific points of high porosity at 15.00 kV (250 x). From image analysis data, the width of particle was 176.4µm. Figure (6b) SEM picture displays prismatic morphology and large particles of carbamazepine (CBZ) with width of particle was 329.5µm at 15.00 kV (500x). However, figure (6c) the photomicrograph reveals the prismatic morphology and the small size of (CBZ) particles with coarse surface and high porosity at 15.00 kV (5.00 x).

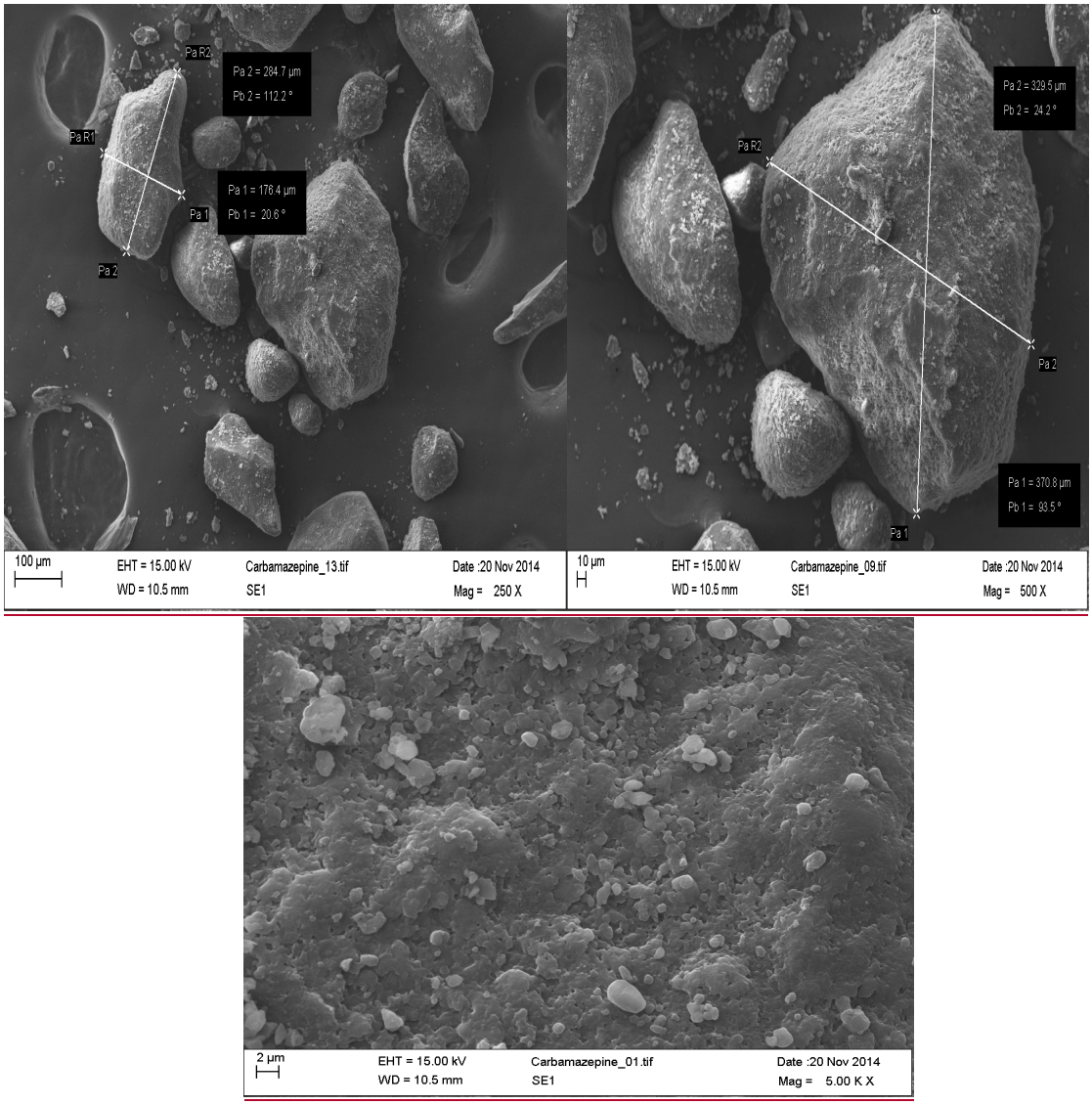

Fig.6 SEM micrographs of the (CBZ) carbamazepine powder particles: magnifications of , (b) 500 times.50(a) times 2

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Based on results of FTIR, DSC and SEM techniques the carbamazepine (CBZ) characterize on other polymorphs with medium intensity bands of FTIR spectra, lower melting point with sharp peak at 191.88 C° with endothermic solid - solid transformation with enthalpy 95,5217 J/g and entropy 4,975 J/g . Moreover, prismatic morphology with rough surface and high porosity at specific points. These results can be used to determine the purity, stability, particle size and identity as well as the amount of carbamazepine drug in sample. From the results, it can be noticed that three techniques are complementary to each other by supplying various information about carbamazepine

CONCLUSION

To sum up, it can be seen the utility of the FTIR, DSC and SEM techniques in identification and characterisation the carbamazepine. In addition, the three instruments were effective techniques to provide whole information about drug which cannot be separately obtained. This information included chemical structure, functional groups such as amine NH2, alkenes, and aromatic rings. Additionally, melting point 191.88 C°, enthalpy 187.96 C° and prismatic morphology with coarse surface also determine amount of carbamazepine in the sample.

Furthermore, it can improve and develop pharmaceutical analysis by defining purpose of analysis, well understanding for analysis process to know all factors which have potential effect on result of process such as instrument setting, process parameters and sample characterizations, ensures selection of the optimal technique and to access accurate results.

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