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Full Length Research Paper

CHARACTERIZATION OF CAPTOPRIL-ETHYL CELLULOSE MICROSPHERES BY THERMAL ANALYSIS

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ABSTRACT

The objective of the present study was to study the physical characterization of Captopril-ethyl cellulose microspheres by thermal analysis such as Differential Scanning Calorimetry (DSC), Differential thermal analysis (DTA) and Thermo gravimetry (TG). Drug polymer interaction can directly affect the dosage form stability, drug encapsulation into polymers and dissolution patterns. In this study thermal analysis has been carried out for the physical mixtures and microspheres of captopril and ethyl cellulose prepared by solvent evaporation method.

Keywords: *DSC, DTG, TG, microspheres, Captopril, ethyl cellulose.*

1. Introduction:

Captopril is used to treat hypertension and heart failure, as it inhibits the activity of angiotensin converting enzyme (ACE). The drug is highly water soluble and has elimination half-life after oral administration of 1.7h [1, 2]. It is stable at pH 1.2 and as the pH increase; the drug becomes unstable and undergoes a degradation reaction [3-5]. Development of controlled release for captopril would bring many advantages for patients [6, 7]. Ethyl cellulose is the most commonly used water insoluble polymer for controlled release formulations [8].

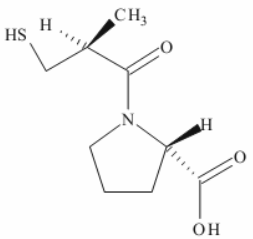

Fig. 1 Structural formula of captopril

Microencapsulation has been used as one of the methods to deliver a drug in a controlled fashion. It provides a means to modify and retard the drug release. Several methods were developed to encapsulate inside microspheres viz solvent evaporation, solvent diffusion, spray drying etc [9-12]. Thermal analysis is a term used to describe the analytical techniques that measure the physical and chemical properties of a sample as a function of temperature or time [13]. Thermal Analysis methods systematically analyze these changes by application of programmed temperature variations for heating and cooling, and by application of specified sample atmospheres and pressures. The properties most often studied are specific heat and enthalpy changes, weight loss or weight gain, Young's modulus, thermal expansion or shrinkage and gas evolution. Differential scanning calorimetry (DSC), Derivative thermo gravimetric analysis (DTG) and thermo gravimetric analysis (TG) are the most common methods of thermal analysis and can rapidly provide significant data on detection of polymorphism and crystallinity, stability (measurement of reaction and decomposition kinetics), assessment of

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interactions/compatibility of dosage form ingredients and glass transition temperature studies. Understanding these properties is very important for a proper development of solid drug products. Thermal analysis is a very frequently used method in the Preformulation tests of solid dosage forms [14, 15].

The aim of the present work was to characterize captopril, ethyl cellulose and microspheres containing captopril by thermal analysis. The interaction of polymer and captopril and characteristics of drug were analyzed using DSC, DTG and TG.

2. Materials and methods:

2.1. Materials:

Captopril was obtained as a gift sample from Akums pharmaceuticals. Ethyl cellulose 8-22cps and acetone LR were procured from S.D. Fine Chem labs (Mumbai). Liquid paraffin was obtained from Ranbaxy fine chemicals (New Delhi) and petroleum ether from Merck Ltd (Mumbai).

2.2. Methods:

2.2.1. Preparation of microspheres:

Microspheres of captopril were prepared by non aqueous solvent evaporation method [16-18]. Polymer solution was prepared by addition of ethyl cellulose in acetone under stirring. To this, the drug was dispersed. The resultant drug-polymer dispersion was poured slowly into liquid paraffin while being stirred at 500rpm by a mechanical stirrer. The solution was stirred continuously for about 3h to allow solvent evaporation. Then the formed microspheres are collected by filtration and washed three times with petroleum ether to remove the residual oil. The collected microspheres are dried for 1h at room temperature and stored in desiccator over fused calcium chloride.

2.2.2. Samples for analysis:

Thermal analysis was carried out for the pure drug (Captopril), polymer (ethyl cellulose), 1:1 ratio physical mixture of drug and polymer and microspheres prepared using drug and polymer.

2.2.3. Thermal analysis:

The thermal analysis (DSC, DTG, and TG) was carried out for drug, polymer, physical mixture of drug and polymer and the microspheres of 1:4 drug-polymer ratio. These investigations were performed on 10.5mg sample using Perkin Elmer (Pyris diamond) instrument, in a nitrogen atmosphere flowing at 200ml/min. Temperature ranged from 23°C until 400°C at a heating rate of 10°C/min was used. 10.5mg of Alumina powder was used as the reference.

3. Results and discussion:

Captopril is a white, crystalline powder. The SEM of the drug and formed microspheres are shown in the Fig: 2. DSC, DTG and TG curves obtained with drug, physical mixture of drug and polymer and microspheres of 1:4 in Fig: 3a, 3b and 3c respectively.

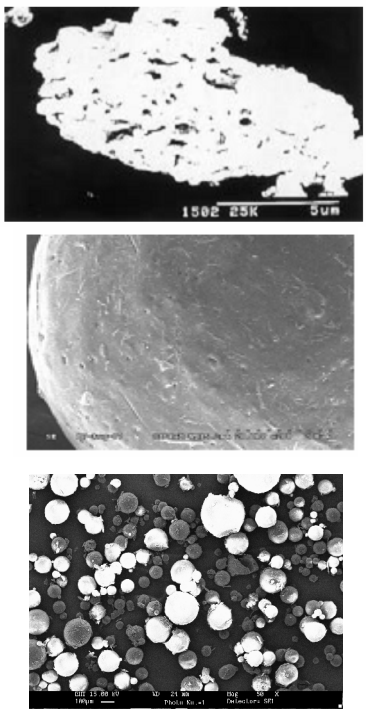

Fig. 2: SEM of drug, placebo and drug loaded microspheres

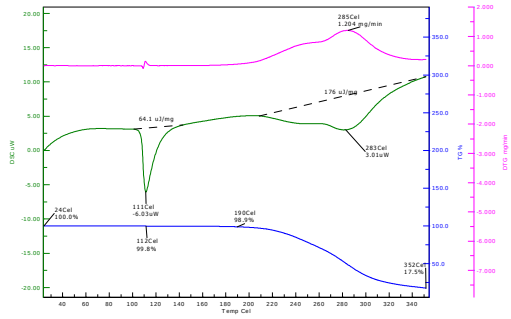

Fig 3a: DTG, DSC, TG of drug

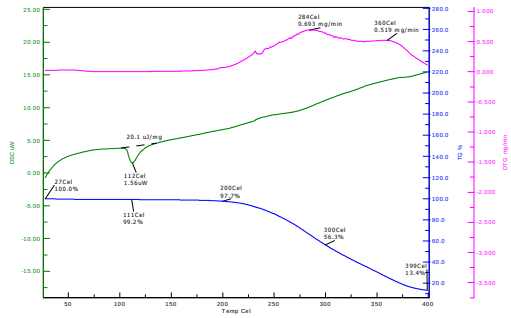

Fig 3b: DTG, DSC, TG of physical mixture

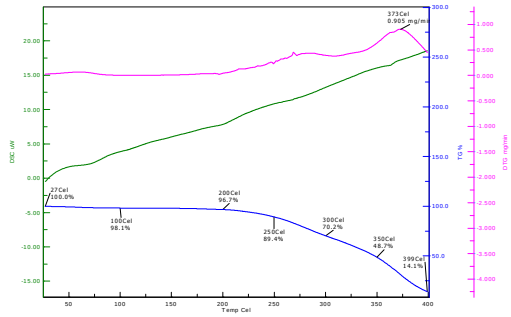

Fig 3c: DTG, DSC, TG of drug loaded microspheres

DSC curve of Captopril shows a sharp endothermic peak that corresponds to melting in the range of 102-130cel with melting temperature of 111cel (Enthalpy change: 64.1uJ/mg). After melting another peak was observed due to thermal decomposition which indicates an endothermic event at the temperature of 283cel (Enthalpy change: 176uJ/mg). The TG/DTG curves of drug indicate the thermal decomposition of Captopril in the following temperature and weight loss of 285cel and 82.5%, 285cel and 1.204 mg/min.

The thermal behavior of physical mixture of Captopril and ethyl cellulose shows the endothermic characteristics of drug, indicating the presumable absence of incompatibility. The fig 3b shows DSC, TG and DTG curves of physical mixture of drug and polymer. The values of peak melting temperature, fusion enthalpy and temperature range of thermal decomposition and weight loss (%) of Captopril, after mixing with polymer and the microspheres are listed in Table: 1.

Sample	Melting temp (cel)	Enthalpy of fusion (uJ/mg)	Decomposition temp (cel)	Enthalpy of decomposition (uJ/mg)	T_{onset} of decomposition (cel)	T_{peak} decomposition (cel)	Weight loss (%)
Captopril	111	64.1	283	176	285	352	82.5
Cap+ethylcellulose (1:1)	112	20.1	-	-	360	399	86.8
Microsphere	-	-	-	-	373	399	85.9

Table 1: Peak temperatures and enthalpy values of drug, physical mixture and microspheres.

It was evident from the DSC profile (fig 3a) that Captopril exhibited a sharp endothermic peak at 111cel, which corresponds to the melting point of the drug. The same DSC profile of the Captopril (fig 3c) appeared at the temperature corresponding to its melting point in the Captopril loaded ethyl cellulose microspheres but with the absence of sharp peak appearance. It appears that there is a significant reduction in the microspheres. The DSC profile of ethyl cellulose did not exhibit endothermic peak at 111cel. This revealed that the drug was compatible and the drug was completely entrapped in the ethyl cellulose microspheres.

4. Conclusion:

The investigated studies supported the evidence for the high potential of thermoanalytical tools for the revelation and characterization of drug and polymer. These results reveal that the drug was compatible with the polymer and neither drug decomposition nor drug-polymer interactions occurred in the freshly prepared microspheres. The shifted peaks suggests that the presence of crystalline nature of the drug was completely absent in the ethyl cellulose microspheres which the drug entrapment inside the polymer.

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