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A review: Analytical method for determination of Azelastine Hcl in pharmaceutical dosage form

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Abstract

Azelastine is among the most frequently used drugs; however, knowledge and solid data about its metabolites are scarcely found in literature. By oxidation of azelastine with H_2O_2, these *N*-oxides were now prepared in racemic form for the first time and were fully characterized. Their structure was additionally confirmed by a single crystal X-ray analysis. Both *N*-oxides were found to be non-cytotoxic in SRB assays.

Keyword:

Instrumentation and methods TGA/DTG and DTA, Differential Scanning Calorimetry (DSC), Mass spectrometry electron impact (MS-EI), Measurement of Entrapment Efficiency, FTIR.

Introduction

Azelastine-HCl, 4-(4-chlorobenzyl)-2-[(4RS)-1- methylhexahydro1H-azepin-4-yl] phthalazin-1(2H)-one hydrochloride [1]. It is an intranasal antihistamine indicated for use in patients with seasonal allergic rhinitis (SAR) and non-allergic vasomotor rhinitis (VMR). It is also used topically in the symptomatic relief of allergic conditions including rhinitis and conjunctivitis[2]. Emedastine difumarate, is 1H-benzimidazole, 1-(2-ethoxyethyl)-2-(hexahydro-4-methyl-1H-1, 4- diazepin-1-yl), (E)-2- butenedioate (1:2) [3]. It is a second generation antihistamine used in eye drops to treat allergic conjunctivitis [4]. The available methods for analysis of azelastine-HCl in pharmaceutical dosage forms and biological fluids are volumetric like UV

spectrophotometry [5], colorimetry , TLC, HPLC, and capillary electrophoresis. Few methods were reported for analysis of emedastine difumarate including only HPLC with tandem MS or radioreceptor assay[6]. Thermal analysis techniques cover all methods in which a physical property is monitored as a function of temperature or time, whilst the sample is being heated or cooled under controlled conditions[7]. Thermogravimetry (TG) and differential scanning calorimetry (DSC) are useful techniques that have been successfully applied in the pharmaceutical industry to reveal important information regarding, the physicochemical properties of drug and excipient molecules such as polymorphism, stability, purity, formulation compatibility among others, and assessing the drug degradation kinetics. There are definitive advantages to employing multiple thermal analysis methods to attain varying views of the physicochemical properties of pharmaceuticals[8]. The determination of the key physical and chemical properties of a new material is essential[9].

Instrumentation and methods TGA/DTG and DTA:

Their curves of drug substances were recorded using Simultaneous Shimadzu Thermogravimetric Analyzer TGA-60 H with TA 60 software in dry nitrogen atmosphere at a flow rate of 30 mL/min in platinum crucible with an empty platinum crucible as a reference[10]. The experiments were performed from ambient temperature up to 1000°C with a heating rate of 8°C/min and 10°C/min for azelastine HCl and emedastine difumarate respectively. The sample mass was about 5 mg of the drug without any further treatment[12]. The kinetic parameters of decomposition such as, activation energy (Ea), frequency factor (A) and reaction order(n) were calculated from TG/ DTG curves. The mathematical models of Horowitz, Metzger and Coats, Redfern were used for kinetic parameters determination[13,14].

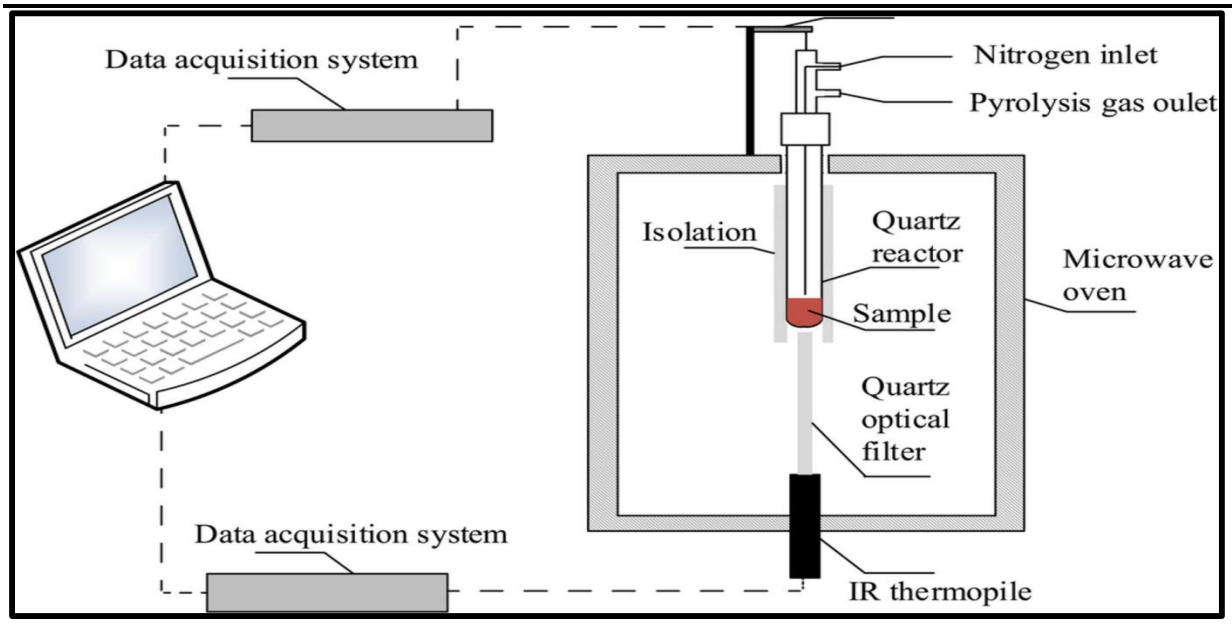

Fig:No:1. Instrumentation and methods TGA/DTG and DTA

Differential Scanning Calorimetry (DSC)

The curves of azelastine hydrochloride and emedastine difumarate were recorded using Shimadzu-DSC 50, in dynamic nitrogen atmosphere with a constant flow of 30 mL/min[16], and heating rate of 2°C/minute, up to temperature 300°C. The sample with a mass of about 2 mg was packed in platinum pan[17]. DSC equipment was preliminarily calibrated with standard reference of indium (99.9%). The purity determination was performed using heating rate of 2°C/minute in the temperature range from 25 to 300°C in nitrogen atmosphere[18].

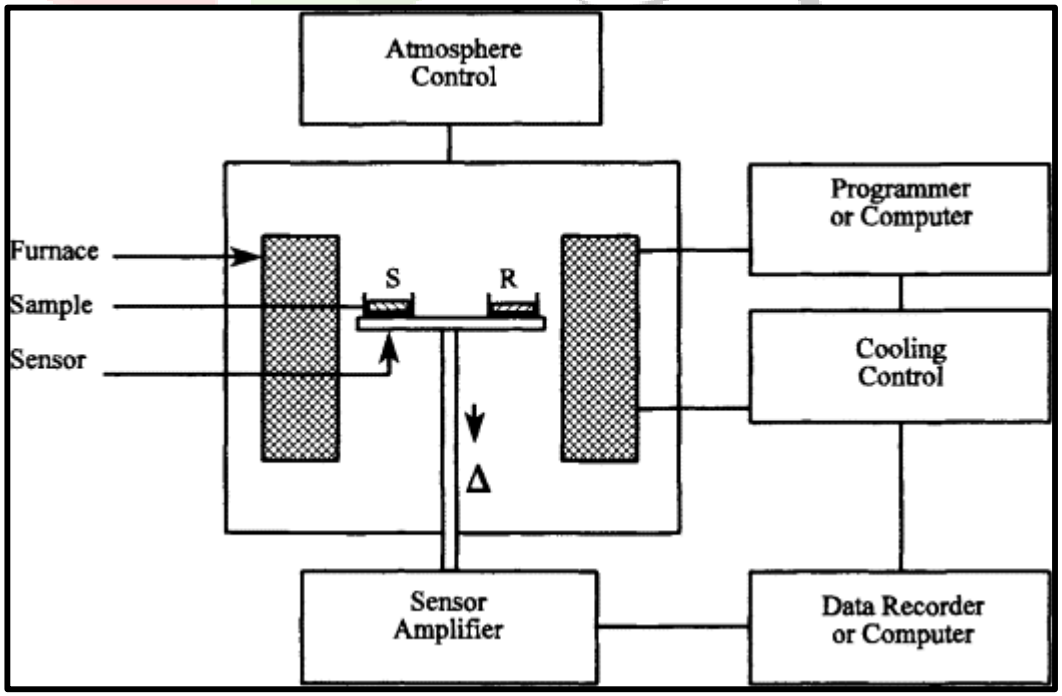

Fig:No:2. Differential Scanning Calorimetry (DSC)

Mass spectrometry electron impact (MS-EI):

Mass spectra of azelastine hydrochloride was recorded using Shimadzu-GC-MS-QP 1000 EX quadruple mass spectrometer with Electron Impact detector equipped with GC-MS data system[19].

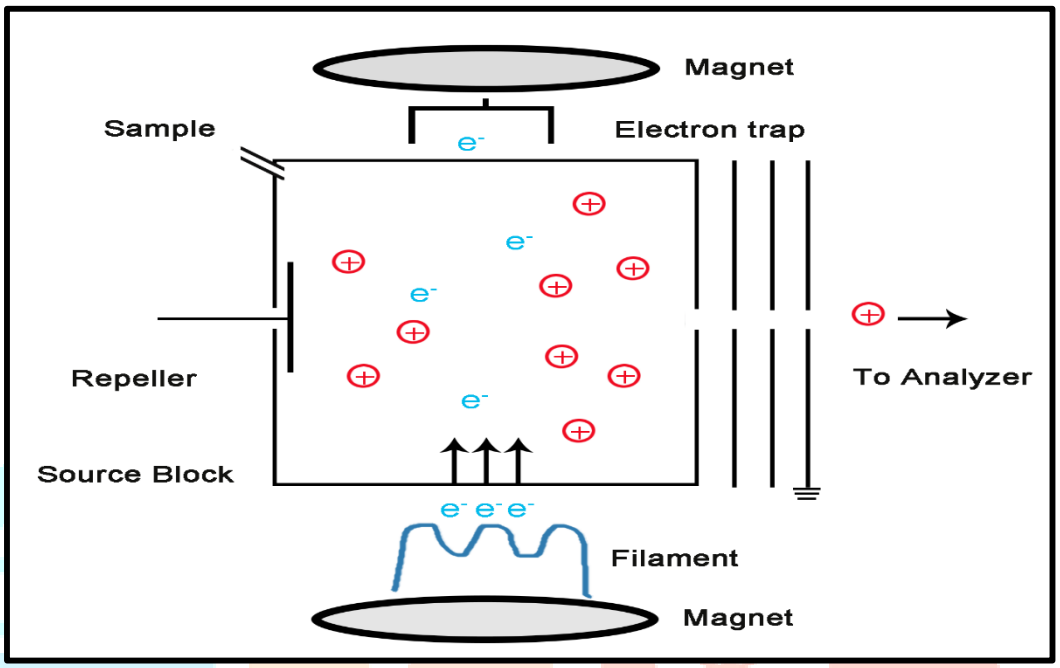

Fig:No:3. Mass spectrometry electron impact (MS-EI):

Melting point:

Opti Melt Automated Melting Point System, SRS Stanford Research System[20].

Differential Scanning Calorimetry Analysis

Differential scanning calorimetry (DSC) analysis was used to characterize the thermal behavior and any possibleinteraction between SA and azelastine HCl. DSC thermograms were obtained using a Perkin-Elmer Pyris 1 DSC[21], equipped withIntracooler 2P cooling accessory. In the present study DSC scans were recorded from 0 to 300 ºC at the rate of10ºC/min.

Measurement of Entrapment Efficiency

For the determination of the entrapment efficiency, the nanoparticles were first separated from the aqueous suspension medium by ultracentrifugation at 30000µg for 45 min[22]. The amount of free AZT in supernatant was measured by validated UV spectrophotometric method at 319 nm. The AZT entrapment efficiency (EE) of nanoparticles was determined in triplicate and calculated as indicated below[23].

FTIR Analysis

As indicated in the IR spectra characteristic peaks of azelastine HCl such as 1599 (NH Bending), 1653(C=N & C=C stretching) and 1732 (C=O stretching) cm-1 are prominently masked in the azelastine HCl loaded nanoparticles[25,26,27]. Change in peak intensity isindicator of chemical and physical changes taking place through ionic gelation and nanoparticles formation processhence it ensured that there was probable interaction between the drug, the SA:CS matrix and CaCl2 at nanoparticles formation and drug entrapment stage; resulting in successful sustained release formulation[28,29].

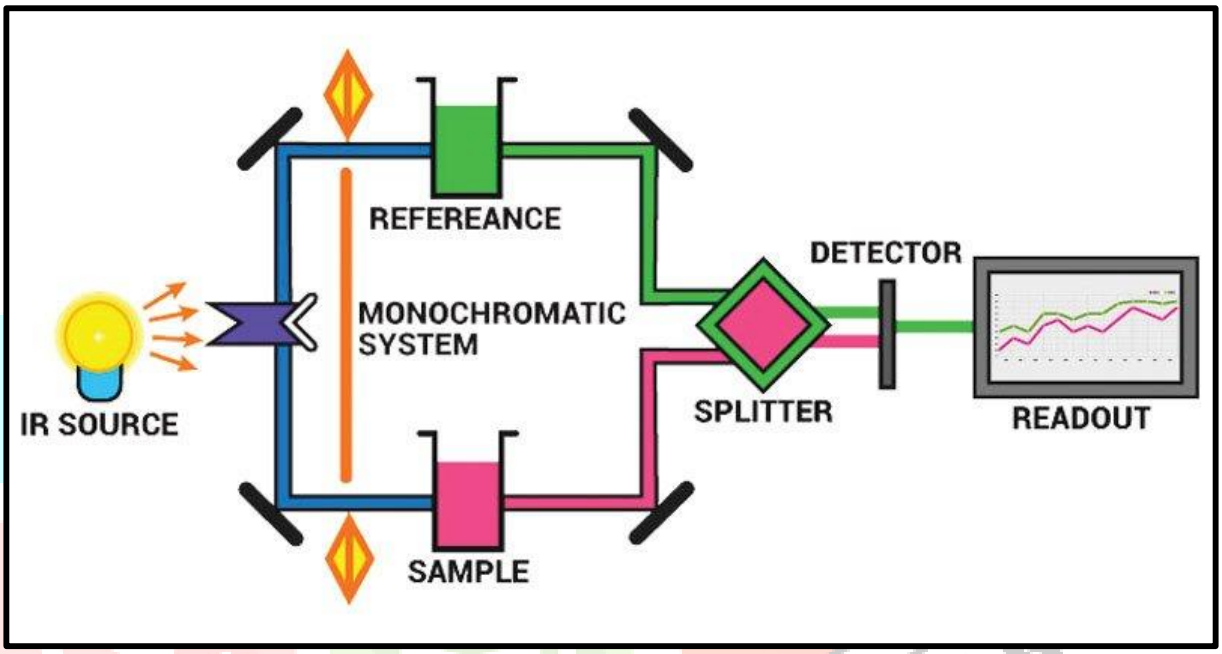

Fig:No:4. FTIR Analysis

CONCLUSION

This method is simple, specific, and easy to perform and requires short time to perform to analyse the samples. The developed method was validated in terms of Linearity, precision, robustness, LOD, LOQ and accuracy. A good linear relationship was observed. The precision results were good enough to indicate that the proposed method was precise and reproducible. The assay experiment showed that the contents of AZT estimated in tablet dosage form were free from the interference of excipients.

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