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Development and Validation of Stability Indicating Uv Spectrophotometric Method For The Estimation Of Teneligliptine In Bulk And Tablet Dosage Form

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ABSTRACT:
A simple, sensitive, accurate, precise, reproducible and cost effective stability indicating UV spectrophotometric method has been developed for quantitative determination of Teneligliptine in bulk and pharmaceutical formulation. The UV spectrum was scanned between 200 to 400 nm and 243 nm was selected as maximum wavelength for absorption. Beer's law was obeyed in the concentration range of 05-25 µg/ml. Good accuracy (100.10-100.20%), precision (%RSD 0.995-0.991) were found, the method was successfully applied to the pharmaceutical dosage form containing the above-mentioned drug without any interference by the excipients. Results of the analysis were validated as per ICH guidelines. Forced degradation studies includes the effect of temperature, oxidation, photolysis and susceptibility to hydrolysis across a wide range of pH values, were carried out according to the ICH requirements which can be used for the routine and quality control analysis of Teneligliptine in raw material and pharmaceutical formulations

Keywords: Teneligliptine, Stability indicating, Forced degradation, Anti-diabetic,

I. INTRODUCTION:

During the pharmaceutical development of a new drug, it is necessary to select as soon as possible the formulation with the best stability characteristics. Regulations regarding stability testing for registration application are provided by current International Commission for Harmonization (ICH), which emphasizes the stress testing conditions with the aim of assessing the effect of severe conditions on the drug in practice, the effects of pH and temperature changes on drug stability are often used in such studies. The results of such studies are of vital importance in the estimation of a drug product shelf life during early stages of its pharmaceutical development. The results may also serve as guides for better drug design, drug formulation and drug analysis.[1]

Teneligliptin is a novel drug, which is used for the treatment of type 2 diabetes mellitus. It is an antidiabetic drug that belongs to dipeptidyl peptidase-4 inhibitors or "gliptins".[2] Chemically, it is {(2S, 4S)-4- [4-(3-methyl-1-phenyl-1H-pyrazol-5-yl)-1-piperazinyl]-2- pyrrolidinyl} (1, 3-thiazolidin-3-yl) methanone. Figure 1 shows that structure of Teneligliptine. Teneligliptin is approved for use in India, Japan, and Korea in 2012.[3] Teneligliptin exerts its activity for 24 h, with elevation of activated glucagon-like peptide 1 (GLP-1) levels by suppressing postprandial hyperglycemia after the meals. Significant decrease in hemoglobin A1c (HbA1c), fasting blood glucose, and postprandial blood glucose levels was observed in type 2 diabetic patients taking teneligliptin for 12 weeks. This drug showed a promising effect in stabilizing the glycemic fluctuations throughout the day and suppressing the diabetic complications.[4,5]

The literature review revealed a simple UV spectroscopic method development and validation of teneligliptin HBr hydrate in tablet dosage form[6], and a stability indicating RP-HPLC method for development and validation of teneligliptin HBr hydrate in pure and tablet dosage for analytical method development.[7,8]

So far, no UV stability indicating method has been reported for the determination of this drug in its pharmaceutical formulations. Among the various methods available for the determination of drugs, spectrophotometry continues to be very popular, because of their simplicity, specificity and low cost.

In the present study a simple, sensitive, selective, inexpensive, accurate and reproducible analytical method with better detection range for estimation of Teneligliptine in pure form and in its pharmaceutical dosage form was developed and

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validated. Based on forced degradation studies, the method was also tested for its stability indicating ability according to the ICH requirements which can be used for the routine and quality control analysis of Teneligliptine in bulk and pharmaceutical formulation.

II. MATERIALS AND METHODS:

Teneligliptine was obtained as a gift sample from Ajanta Pharma Limited, Mumbai, India. All solvents and other chemicals used were of analytical reagent grade purchased from Research lab, Mumbai. A Lab India UV/VIS double beam spectrophotometer (model 3000+) with 1 cm matched quartz cells was used for all spectral measurements. Double distilled water used throughout the experiment.

(i) Preparation of standard stock solution

10 mg of Teneligliptine was accurately weighed and transferred to 100 ml volumetric flask and dissolved in about 20 ml of distilled water. The volume was made up to the mark with distilled water to give 100 µg/ml stock solution.

(ii) Preparation of calibration curve for Teneligliptine

By scanning a suitable standard solution in the UV-VIS spectrophotometer in the wavelength range of 200-400 nm, the λ max of the drug was determined, shown in figure 2. Aliquots (1, 2, …. 5 ml) from standard solution of Teneligliptine were pipetted out in to a series of five volumetric flasks and the volume was made up to 10 ml with double distilled water. The absorbance was measured at 243 nm against reagent blank. The calibration curve was constructed by plotting absorbance v/s concentration (µg/ml). Correlation coefficient was also measured. The summary of analytical parameters and calibration curve data are presented in Table 1 and Table 2 respectively.

(iii) Estimation of Teneligliptine

Twenty tablets of Tenure® (Glenmark pharmaceutical Ltd.) were weighed accurately and powdered. Powder equivalent to 50 mg teneligliptin HBr hydrate was weighed and transferred to a 100 ml volumetric flask. It was dissolved in 100 ml distilled water and sonicate for 15 minutes to get a homogeneous solution. Then it was first filtered through a 0.45µm Whatman filter paper. A final concentration of 100 µg/ml of teneligliptin was prepared. This solution was filtered through filter paper to remove some un-dissolved excipients. After filtration, from this 2 ml was taken and diluted to 10 ml with distilled water which gives 20 µg/ml solution and the absorbance of the solution was measured at 243 nm.

(iv) Method Validation

The method was validated according to ICH Q2B guidelines to determine the Linearity, sensitivity, precision, and accuracy of the analyte.[9]

Linearity of the proposed method was determined by measuring the absorbance of the standard solutions in the concentration range of 5-25 µg/ml and performing least square regression analysis. In addition, the accuracy of the proposed method was checked using standard addition method and recovery studies were carried out at 80%, 100% and 120% of target concentration. The percent analytical recovery was calculated by comparing the concentration resulted with the addition of spiked samples with actual expected theoretical increase in concentration. Intra-day precision was determined by carrying out the analysis for six concentrations at two different time interval in a day. Similarly interday precision was determined by performing analysis on two consecutive days. LOD and LOQ of the proposed methods were calculated.[10] Recovery of the analyte of interest from a given matrix can be used as a measure of the accuracy or the bias of the method.[11]

(v) Stability Studies of Teneligliptine

Stability studies were performed by forced degradation study of Teneligliptine and it includes the study of effect of temperature, oxidation, photolysis and susceptibility to hydrolysis across a wide range of pH values. For acidic hydrolysis 0.1, 1.0 N HCl, for basic hydrolysis 0.1, 1 N NaOH, for oxidation study 0.1%, 1% and 3% H_2O_2 was used. For carrying out photolysis studies the drug was treated with sunlight for 3 days and thermal stress was applied by heating the drug at 60^0C for 2 hrs.

III. RESULTS AND DISCUSSION:

The development of a simple, economic, rapid, sensitive, and accurate analytical method for the routine quantitative determination of samples will reduce unnecessary tedious sample preparations and the cost of materials and labor. The absorption spectrum of Teneligliptine in double distilled water is shown in (Fig 2).

The λ max of the drug for analysis was determined (243 nm) by taking scans of the drug sample solutions in the entire UV region. Calibration curve data was constructed in the range of the expected concentrations of 5-25 µg/ml. Beer's law was obeyed over this concentration range (fig 3). Overlain spectra for 5-25 µg/ml concentrations shown in (Fig 4).

The regression equation was found to be Y=0.0257x+0.0281. The correlation coefficient (r) of the standard curve was found to be 0.9991. The characteristic of the calibration plot is presented in

Table 1. Performing replicate analyses of the standard solutions was used to assess the accuracy and precision of the proposed methods (Table 3 and 4). The LOD and LOQ were found to be 0.19µg/ml and 0.83 µg/ml respectively.

To study the accuracy of the proposed method and to check the interference from excipients used in dosage forms, recovery experiments were carried out by the standard addition method. The mean recovery was found to be 100.10-100.20. The proposed methods can be successfully applied for assay in tablet dosage forms without any interference (Table 3).

The selected concentration within the calibration range was prepared in double distilled water and analyzed with the relevant calibration curves to determine the intra- and inter-day variability.

To determine the precision of the method Teneligliptine solutions at concentration 05, 15, 25 µg/ml were analyzed each in triplicate. Solutions for the standard curves were prepared fresh everyday. The method was found to be precise. The % RSD values for interday precision at concentration 05, 15, 25 µg/ml was found to be 0.995, 0.012, 0.991 respectively and for intraday precision it was 0.451, 0.320, 0.128 respectively. Results are shown in Table 4.

The application of this procedure is explained in the experimental section. The obtained results demonstrate the validity and accuracy of the proposed method for the determination of Teneligliptine in sachets. The stability studies indicates that appreciable changes were observed by treating the drug with sun light, thermal stress, oxidation, acid and basic hydrolysis, however there was appreciable change with all these stress conditions. The results are shown in Table 5.

These results reveal that the developed method was simple, sensitive, sensitive, inexpensive, accurate and reproducible and consequently, can be applied to the determination of Teneligliptine tablet in pharmaceuticals without any interference from the excipients. Based on forced degradation studies according to the ICH requirements, this method can be used for the routine and quality control analysis of Teneligliptine in raw material and pharmaceutical formulations.

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