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METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF TENELIGLIPTIN IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Simple, accurate, precise and economical HPLC method has been developed and validated for the estimation of teneligliptin hydrobromide hydrate (THH) in bulk and tablet dosage form. Separation was achieved on a Prontosil C_8 column using a mobile phase consisting of Acetonitrile: Dihydrogen Potassium Phosphate buffer in 60:40 (v/v) adjusted with o-phosphoric acid pH 3.0.Gradient elution at a flow rate of 1ml/min and UV detection at 246nm. Linearity was observed in the concentration range of 30-150 µg/ml. The retention time for Teneligliptin was 2.47 min. The proposed methods were validated according to the ICH guidelines. The developed methods are accurate and precise and can be used for routine quality control analysis of Teneligliptin in bulk and pharmaceutical formulation.

KEYWORDS: Teneligliptin, Method development and validation, UV, Spectrophotometric.

INTRODUCTION

Teneligliptin is mainly use for the treatment of Type-II diabetes mellitus. It is a highly potent, competitive and long-lasting DPP-4 inhibitor that improves postprandial hyperglycemia and dyslipidemia. Teneligliptin chemically described as Figure no-1.[(2S, 4S)-[-(3-Methyl-2-Phenylpyrozol-3-yl)Piperazin-1-yl] Pyrrolidin-2-[1, 3 Thiazolidin-3-yl)Methanone. Recent studies have revealed that this drug is unique in its nature and exhibits multiple pharmacological effects. It includes vasoprotective, neuroprotective effects. (Dipeptidyl peptidase 4, EC 3.4.14.5) which is involved in the inactivation of the incretin hormones

(glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). These incretin hormones are rapidly degraded by the enzyme DPP-4. Both incretin hormones are involved in the physiological regulation of glucose homeostasis. GLP-1 and GIP are secreted by the intestine at a low basal level throughout the day and concentrations are increased in response to a meal. GLP-1 and GIP increase insulin biosynthesis and secretion from pancreatic beta cells in the presence of normal and elevated blood glucose levels. Furthermore GLP-1 also reduces glucagon secretion from pancreatic alpha cells, resulting in a reduction in hepatic glucose production. Teneligliptin binds to DPP-4 in a reversible manner and thus leads to an increase and a prolongation of active incretin levels. Teneligliptin glucose dependently increases insulin secretion and lowers glucagon secretion thus resulting in an overall improvement in the glucose homoeostasis.

Literature survey revealed reported method by HPLC for analysis of Teneligliptin hydrobromide hydrate. Also analytical method for quantification of teneligliptin in plasma has been reported. The purpose of present work is to develop simple, precise, less time consuming, selective and economic high-performance liquid chromatographic method for determination of Teneligliptin hydrobromide hydrate in bulk and tablet dosage form. The proposed methods were validated as per ICH guidelines.[7] Structure of teneligliptin hydrobromide is shown in Fig. 1.

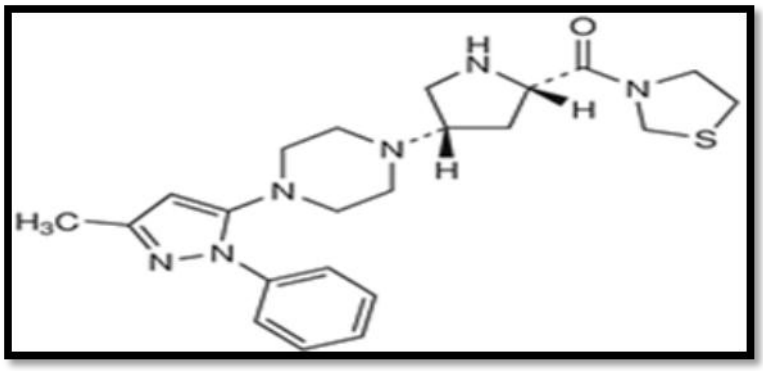

Fig no -1: Structure of teneligliptin hydrobromide.

MATERIAL AND METHODS

Chemicals and Reagents

Teneligliptin HBr bulk drug was obtained from Lupin Pvt LTD, (pune, India). The commercially available tablets of Teneligliptin HBr were purchased form Indian market (Tendia tablets).

Standard stock solution

Teneligliptin (10 mg) was dissolved in 10 ml of volumetric flask and volume was made up to the mark to obtained 1000 µg/ml solution. From above stock solution pipette out 1ml solution and adjust the volume in 10 ml volumetric flask to obtained 100µg/ml. The stock was diluted with Diluents to get required concentrations.

Preparation of mobile phases

Mobile phase used in a combination of 60:40v/v of Acetonitrile: 0.025M Potassium Dihydrogen Phosphate Buffer (pH3.0). Mobile phase was filtered through 0.45µm membrane filter and sonicated for 15 minute to degas.

Preparation of Test sample

Weigh twenty tablets and crushed into fine powder. A potion equivalent to about 10mg of Teneligliptin was accurately weighed and transferred to a 10mL volumetric flask. The volumetric flask was sonicated for 20 min to effect complete dissolution of drug, the solution were then made up to volume with diluent to obtain a standard stock solution (1000µg/mL). The solution was filtered through 0.45µm nylon filter. An aliquot was diluted to 10mL with diluent to obtain a working standard solution of standard drug (100µg/mL).The solution was diluted with diluent to obtain sample solution of drug (10µg/mL). Each solution was injected and chromatographed in triplicate. The chromatograms were recorded and peak area of Teneligliptin was measured at 246 nm. Amount for drug (in mg/tablet) was estimated by comparing mean peak area of sample with that of the standard and percent label claim was calculated.

Table No.1: Result of tablet analysis

Brand Name of tablet	Mean*	SD	%RSD
Tendia	101.2	0.140	0.139

*Average of five determinations.

Selection of analytical wavelength

Aliquot portion of standard stock solution was appropriately diluted with mobile phase to obtain final concentration of 30µg/ml of Teneligliptin. The solution was scanned using double beam UV-Visible Spectrophotometer-1800 in the spectrum mode between the wavelength ranges of 400 nm to 200 nm against mobile phase as blank. The wavelength

selected was 246 nm as Teneligliptin showed significant absorbance at this wavelength. Typical chromatogram obtained is shown in Fig. 2.

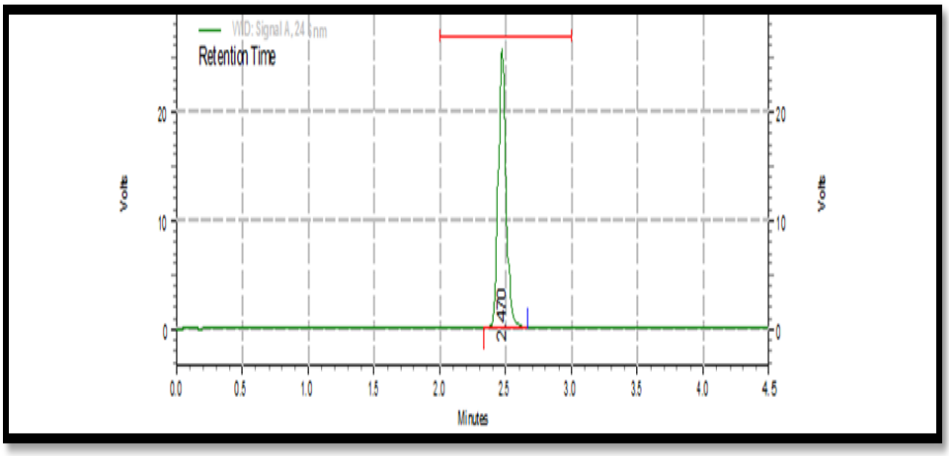

Fig 2: Typical chromatogram of Teneligliptin.

Calibration plot for Teneligliptin hydrobromide

Accurately weighed quantity (10 mg) of Teneligliptin, was transferred to 100.0 ml volumetric flask, added 40 ml of mobile phase and ultrasonicated for 10 minutes, volume was then made up to the mark with mobile phase. Aliquot were prepared and diluted to mobile phase. The diluted solutions were injected (3µl) into the HPLC system and chromatographed using optimum chromatographic conditions. The peak area of TH was measured at 246 nm. Each solution was injected and chromatographed in triplicate. Mean peak areas were calculated for each drug concentration.

Method validation

The method was validated in compliance with ICH guidelines.

Linearity

Peak areas were found to have good linear relationship with the concentration. Teneligliptin hydrobromide hydrate was found to give linear detector response in the concentration range of 30-150 µg/ml (shown in Fig.3). The straight line equation and coefficient of correlation for Teneligliptin calibration curve was y =57840x+ 88407and r^2 = 0.9992 respectively.

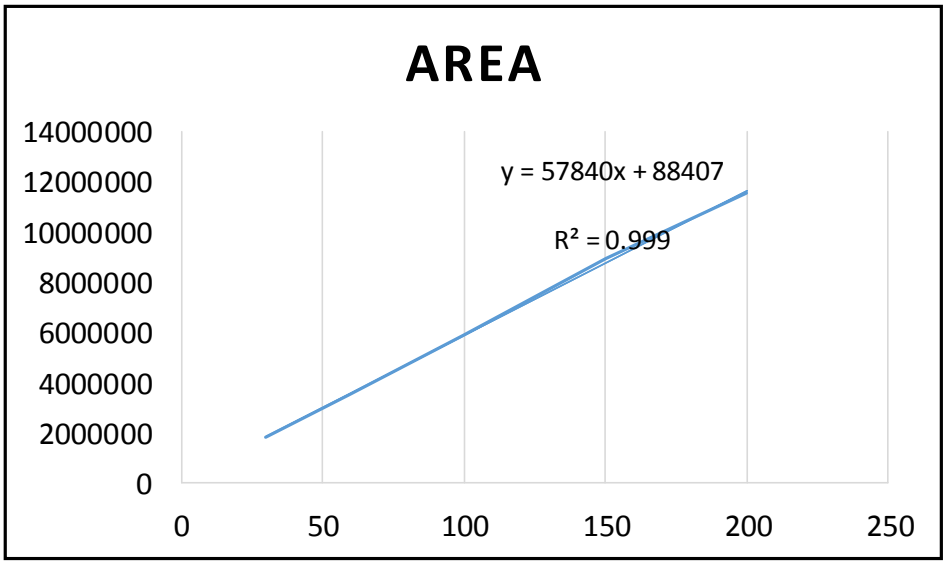

Fig. 3: Calibration curve of Teneligliptin at 246 nm.

Accuracy

The accuracy of proposed method was ascertained on the basis of recovery studies. Weighed the pre-analyzed tablet powder equivalent to 10mg; a known amounts of standard drug was added at different levels 80-120%. The resultant solutions were then re-analyzed by the developed methods. At each concentration, each sample was analyzed thrice at each level to check repeatability and from the obtained data it was analyzed that the proposed methods were found to accurate.

Table No.2: Results of Accuracy.

Level of addition	% Mean recovery*	SD	% RSD
80%	98.4	0.2547	0.2588
100%	99.8	0.6632	0.6644
120%	100.3	0.1210	0.1206

Precision

The precision of the analytical method expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. The precision of the methods can be studied as; intra-day variation, inter-day variation studies and results were expressed as SD and % RSD of series of measurements.

Table No.3: Results of Intraday.

Amount(µg/ml)	SD	%RSD*
30	0.43	0.436
60	0.42	0.429
90	0.44	0.442

Table No.4: Results of Interday

Amount(µg/ml)	SD	%RSD*
30	0.48	0.483
60	0.64	0.647
90	0.58	0.582

Limit of Detection (LOD) and Limit of Quantitation (LOQ)

LOD and LOQ values for Teneligliptin was found to be 0.176 and 0.534 µg/ml, respectively. The low LOD and LOQ values for Teneligliptin indicate the sensitivity of the method.

Ruggedness

Ruggedness of proposed methods was performed to examine effect of non-procedure related factors such as instruments and analysts. For this study, Teneligliptin (150µg/mL) was analyzed by proposed methods using two different analyst and two different instruments, restraining similar operational and environmental conditions.

Table No.5: Results of Ruggedness.

Sr.No	Analyst	Conc.(µg/ml)	SD	% RSD
1	Analyst-I	150	0.2911	0.00887
2	Analyst-II	150	0.2922	0.00873

Robustness

To evaluate the robustness of the proposed method, small but deliberate variations in the optimized method parameters were done. The effect of changes in temperature was studied. The mobile phase composition was changed in ± 2ml proportion and the flow rate was varied by ± 0.1 ml/min, of optimized chromatographic condition. The solution containing Teneligliptin was injected into the HPLC system and chromatographed under varied conditions.

Table No.6: Results of Robustness

Sr.No	Parameter	Temperature	Conc(µg/ml)	SD	%RSD
1	Change in temperature	26.2^0C	30	0.2886	0.856
2		23.7^0C	30	0.278	0.865

Specificity

For the specificity study the sample may be spiked with excipients or possible interfering components. In case of impurity tests, method is said to be specific only if it can be determined the analyte in presence of interference.

Table No.7: Results of Specificity.

Level addition	Tablet drug conc. (µg/ml)	Amount of excipients added (µg/ml)	%RSD
80%	12	15	0.1149
100%	15	15	0.1296
120%	18	15	0.0133

*****Average of three determination

CONCLUSION

The results obtained it is concluded that the method is sensitive, accurate, precise and reproducible, where teneligliptin hydrobromide hydrate can be determined in bulk and in pharmaceutical formulation without interference from the excipients. The proposed HPLC method gave sharp peak for Teneligliptin and complies system suitability parameters. ICH guidelines were followed throughout method validation and the suggested method can be applied for routine quality control analysis of pharmaceutical formulation containing the drug. The HPLC method can be further extended to characterize the structure of the degradation products.

REFERENCES

1. Kishimoto M. Teneligliptin: a DPP-4 inhibitor for the treatment of type 2 diabetes, Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 2013; 6: 187–195.
2. Patel BD, Ghate MD. Recent approaches to medicinal chemistry and therapeutic potential of dipeptidyl peptidase-4 (DPP-4) inhibitors, European Journal of Medicinal Chemistry, 2014; 74: 1-32.
3. Kutho E, Hirate M, Ikeno Y. Teneligliptin as an initial therapy for newly diagnosed, drug native subjects with type II diabetes, J Clin Med Res, 2014; 6(4): 287-294.
4. Yoshida T, Akahoshi F, Sakashita H et al. Discovery and preclinical profile of teneligliptin (3-[(2S,4S)-4-[4-(3-methyl-1-phenyl-1H-pyrazol-5-yl)piperazin-1-yl]pyrrolidin-2-ylcarbonyl]thiazolidine): A highly potent, selective, long-lasting and orally active dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes. Bioorg Med Chem, 2012 Oct 1; 20(19): 5705-19.

5. Eto T, Inoue S, Kadowaki T. Effects of once-daily teneligliptin on 24-h blood glucose control and safety in Japanese patients with type 2 diabetes mellitus: a 4-week, randomized, double-blind, placebo-controlled trial. Diabetes Obes Metab, 2012 Nov; 14(11): 1040-6.
6. ICH Harmonized Tripartite guidelines, Validation of Analytical Procedure: Text and Methodology, Q2 (R1), Geneva 2005; 1-13.
7. Goda M, Kadowaki T, Teneligliptin for treatment of type 2 diabetes, PUB. MED, 2013; 49(10): 615-29.
8. Ryuichi M, Hironori N. Teneligliptin: expectations for its pleiotropic action. Expert Opinion on Pharmacotherapy, 2015; 16(3): 417-426.
9. Sonawane A M, Dhokale K K, Randhe V A.A Simple UV-Spectrophotometric Method Development and Validation of Teneligliptin in Tablet Dosage Form, Indo American J Pharm. Res, 2016; 6(4): 5219-5224.
10. Bronson J, Black A, Murali Dhar TG, Ellsworth BA, Robert Merritt J. Teneligliptin(antidiabetic), chapter: to market, to market—2012. Annu Rep Med Chem, 2013; 48: 523–4.