WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 5, 1625-1632. Research Article ISSN 2277– 7105

SPECTROPHOTOMETRIC DETERMINATION OF AN ANTIDIABETIC DRUG TENELIGLIPTIN BULK AND PHARMACEUTICAL FORMULATIONS

Manjusha D. Karad and V. D. Barhate*

Department of Chemistry, VES College of Arts Science and commerce, Chembur Mumbai 400071, India.

Article Received on
14 March 2016,
Revised on 05 April 2016,
Accepted on 26 April 2016
DOI: 10.20959/wjpr20165-6222

***Corresponding Author**
V. D. Barhate
Department of Chemistry,
VES College of Arts
Science and commerce,
Chembur Mumbai 400071,
India

ABSTRACT

A new, simple, precise, sensitive, accurate, and reproducible spectrophotometric method have been developed for the determination of Teneligliptin in pure and dosage forms. Method is based on oxidation of the drug with 1, 10 phenanthroline producing orange colored chromogen which is measured at 510 nm. Beer's law is obeyed in the concentration range of 0.5 - 4.0 µg/mL for the developed method. The molar absorptivity and Sandell's sensitivity are found to be 19117.57 L $mol^{-1}cm^{-1}$and 0.033 µg/cm^2 respectively. The regression equation for Teneligliptin was found to be y = 0.1376 X + 0.0354 and the correlation coefficient for the regression line was 0.9973. Different experimental parameters affecting the color development and stability of colored product are carefully studied and optimized. The developed method could be successfully applied to pharmaceutical formulations. The results obtained are in good agreement with those obtained using standard method.

KEYWORDS: Teneligliptin, Spectrophotometric method, DPP-4 inhibitor, diabetes, 1, 10-phenanthroline (O-PHEN), Teneglyn Marketed formulation.

INTRODUCTION

Teniligliptin is chemically described as {(2S, 4S)-4-[4-(3-Methyl-1-phenyl-1H-pyrazol-5-yl) piperazin-1-yl] pyrrolidin-2-yl} (1,3-thiazolidin-3-yl) methanone hemipentahydrobromide hydrate. Teneligliptin hydrobromide hydrate is a dipeptidyl peptidase 4 (DPP4) inhibitor is highly effective in lowering blood glucose levels. Teneligliptin hydrobromi hydrate is a highly potent, competitive, and long-lasting DPP-4 inhibitor that improves postprandial

hyperglycemia and dyslipidemia.[1,2,3,4] This drug inhibits the enzyme dipeptidyl peptidase-4 which degrades incretin, a hormone adjusting blood glucose level. Consequently, it enhances insulin secretion depending on blood glucose level, and improves blood glucose control. It is effectively used to treat type 2 diabetes mellitus. The most commonly reported adverse reactions include hypoglycemia, constipation, feeling of enlarged abdomen , abdominal discomfort, nausea, abdominal pain, meteorism, stomatitis, eczema, rash, pruritus, dermatitis and malaise. Literature survey reveals that very few HPLC methods have been reported for the estimation of Teneligliptin hydrobromide hydrate in pure and tablet dosage forms.The aim of the present work is to develop simple accurate, precise and validated method for determination of teneligliptin in tablets, which therefore serves as a tool for the quality control of pharmaceutical dosage forms.

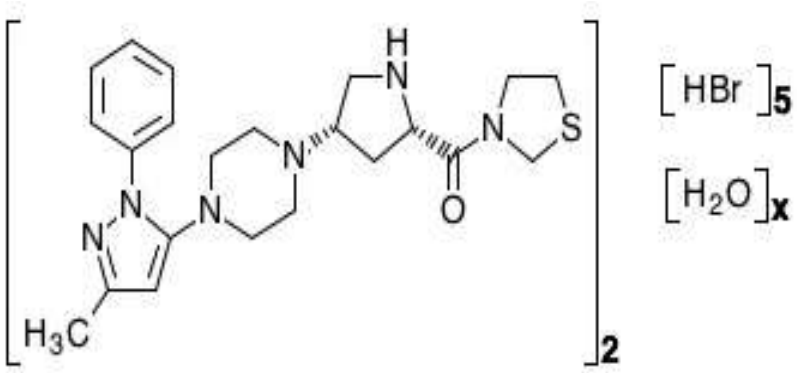


Figure 1: Molecular structure of Teniligliptin hydrobromide hydrate

EXPERIMENTAL

Instrumentation: An ELICO SL-159 model, 2nm high resolution, double beam, 1cm length quartz coated optics; Wavelength range190-1100nm; High stability, linearity, precision instrument is used for all the spectral measurements. All chemicals and reagents used in the analysis are of analytical grade and doubly distilled water is used for the preparation of all the solutions.

MATERIALS AND METHODS

Preparation of Standard solution of drug: An accurately weighed 20 mg of teneligliptin is dissolved in 50 ml of methanol .The final volume is adjusted with methanol (1:1) to 100ml in standard flask. Working solution prepared by suitable dilution of this solution.

Preparation of Reagents: 0.241%(w/v)Fe (III) solution is prepared by dissolving 241mg of anhydrous ferric ammonium sulphate in 100mL of double distilled water, 0.991% (w/v) o-

phenanthroline is prepared by dissolving 991mg of the reagent in 100mL of alcohol and 0.15% (v/v) O-phosphoric acid solution is prepared by diluting 1.5 mL of laboratory reagent (AR Grade) of o-phosphoric acid to 1000mL with distilled water.

Experimental Procedure: Different portions (1.0- 8.0 mL, 0.5µg/mL) of standard teneligliptin solution is delivered into a series of 25mL calibrated standard flask and then 2.0 mL of $5.0x10^{-3}$M of Fe (III) solution, 2.0mL of $5.0x10^{-2}$M o-phenanthroline are added successively. The total volume in each flask is brought to 16 mL with distilled water. The flasks are kept on a boiling water bath for 20 minutes. The flasks are removed and cooled to room temperature.3.0 mL of $2.0x10^{-2}$M of o-phosphoric acid is added and volume in each flask is made up to the mark with distilled water.The absorbance of the colored complex solution is measured after 5 minutes against a reagent blank prepared at 510 nm (Fig.1 A). The amount of the teneligliptin is computed from the appropriate calibration graph (Fig.2).

Analysis of pharmaceutical sample: Tablets powdered equivalent to 20 mg of the drug is weighed accurately and transferred into 250ml beaker and shaken with 50 ml methanol and solution is filtered into 100ml standard flask, wash with methanol (1:1) and volume is adjusted with methanol (1:1). Suitable aliquots of this solution used for the determination of teneligliptin contents by procedure describe earlier.

Absorption spectra: The absorbance of the colored complex solution is measured after against a reagent blank prepared similarly except drug from 350 to 630 nm and maximum absorbance is found to be at 510 nm.

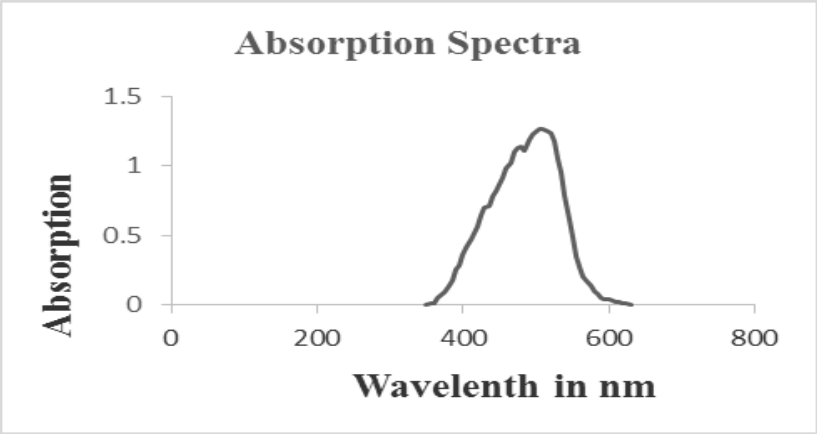


Fig.-1A: Absorption spectra teneligliptin with Fe (III) /O-PHEN

Calibration curve

The calibration curve is plotted between absorbance values and amount of drug (concentration of drug). The calibration curve is found to be linear over a concentration range of 0.5 to 4.0 µg/ml of teneligliptin.

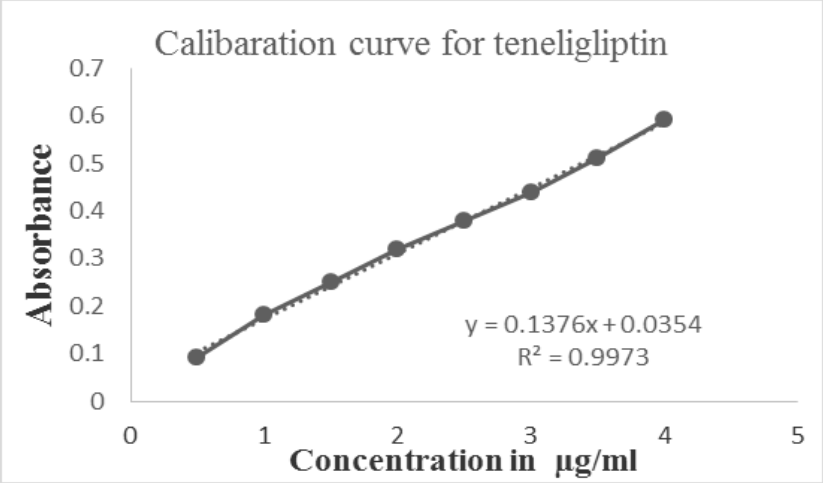


Fig.-2: Linear plot of teneligliptin with Fe (III)/O-PHEN

Effect of heating time

It is observed that 15 mimutes are sufficient for full colour development hence we have selected 20 minutes time for further studies.

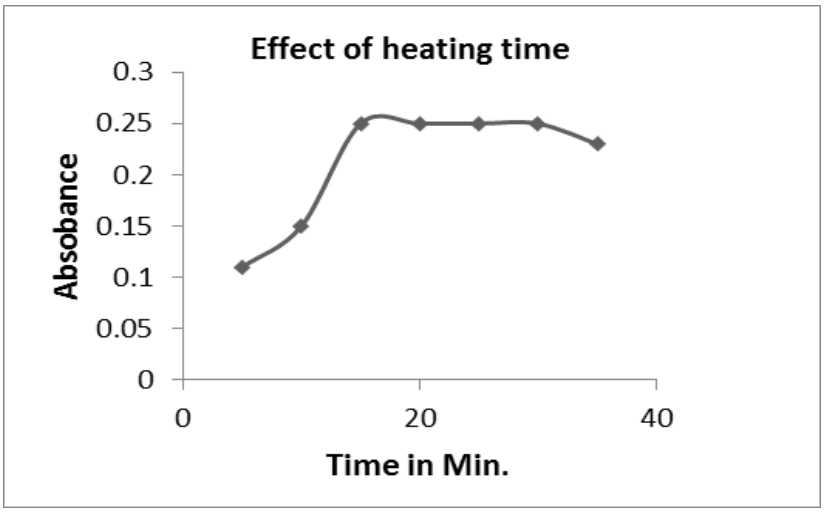


Fig.3 Effect of heating time

Effect of concentration of H_3PO_4

Absorbance remains constant after 1.5 mLof 0.02M H_3PO_4.Hence 2 .0 mLof 0.02M H_3PO_4 is used for colour development and further studies.

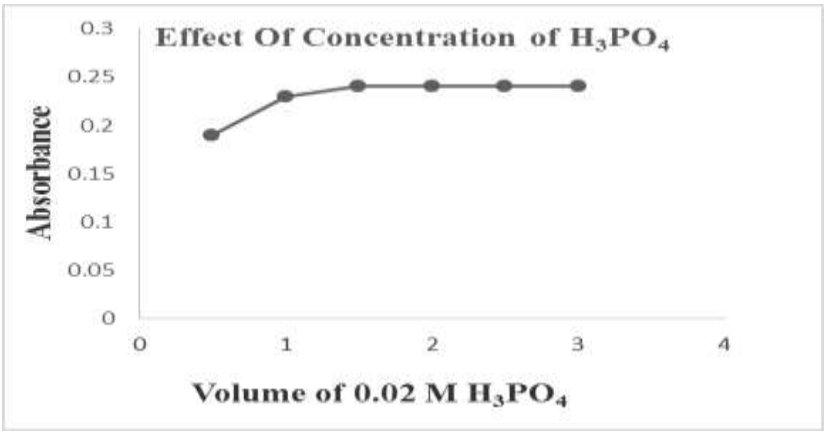
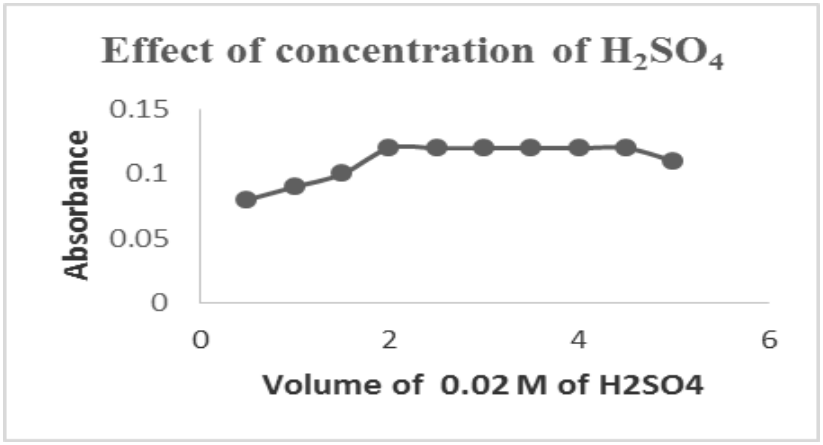


Fig.4 Effect of concentration of H_3PO_4

Effect of concentration of H_2SO_4: Since lower absorbance values are observed for the study of effect of concentration of **H_2SO_4** Hence H_3PO_4 is used for further studies.



Effect of concentration of 1,10 phenanthroline

It is observed that absorbance remains constant after 0.04 M concentration of 1,10 phenanthroline.we have is used 0.05 M for colour development and further studies.

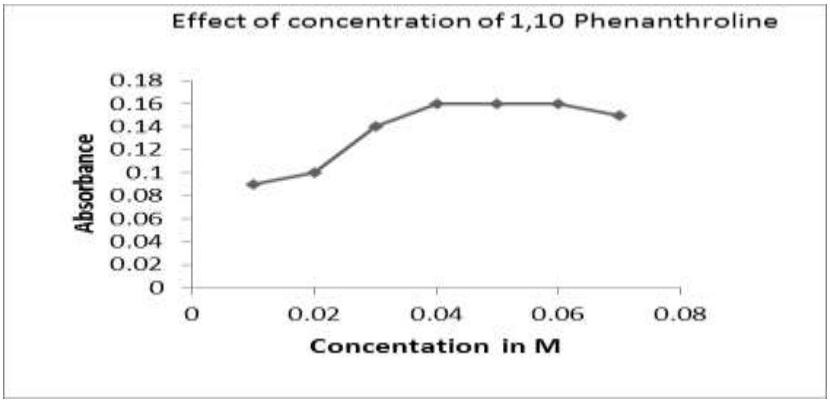


Fig.5 Effect of concentration of 1, 10 phenanthroline on absorbance of developed system.

RESULTS AND DISCUSSION

In order to test whether the colored product formed in this method adhere to Beer's law, the absorbance at maximum wavelength of a series of eight concentrations are plotted against concentration of the drug in µg/mL (Fig2). Beer's law is obeyed within the limits 0.5 - 4.0 µg/mL of teneligliptin, molar absorptivity and Sandell's Sensitivity is found to be19117.57 L $mol^{-1}cm^{-1}$and 0.033 µg/cm^2. Regression analysis of the Beer's law plots at λ_{max} reveals a good correlation. The graphs show negligible intercept and are described by the regression equation y = 0.1376 X+ 0.0354 and the correlation coefficient for the regression line was 0.9973.(where Y is the absorbance of 1 cm layer, b is the slope, a is the intercept and C is the concentration of the measured solution in µg/mL). The high molar absorptivity of the resulting colored complex indicate the high sensitivity of the method.

Precision of the developed method is ascertained from the absorbance values obtained by actual determination of ten replicates of a fixed amount of the test in total solution. The percent of relative standard deviation and Variation from mean at 95% level confidence limit percent are calculated for the developed method. To determine the accuracy of the method, three different amounts of drug sample within the linearity limits are prepared and analyzed by the developed method. The percent recoveries of the drug by this method is found to be within the range which indicates that the developed method is accurate. Optical characteristics, linear regression parameters, precision and accuracy of the proposed method is shown in Table-1. The method have been successfully applied for the determination of teneligliptin in pharmaceutical preparations.

Table-1; Optical characteristics, Regression parameters, Precision and Accuracy of the proposed method

Parameters	Results
Maximum Wavelength λ_{max}	510 nm
Beer's Law Limits µg/mL	0.5-4.0 µg/mL
Sandell's Sensitivity (µg/cm^2 /0.0001 Absorbance)	0.033 µg/cm^2
Molar Absorptivity L $mol^{-1}cm^{-1}$	19117.57 L $mol^{-1}cm^{-1}$
Slope(b)[a]	0.1376
Intercept(a)[a]	0.0354
Standard Deviation on intercept(S_a)	0.001763
Standard Deviation on slope (S_b)	0.001153
Correlation Coefficient (r)	0.9973
Standard Deviation (S)	0.5165
%RSD	2.06

Variation from mean at 95% level confidence limit	±0.3692
Limit of Detection (LOD)µg/Ml	0.04187
Limit of Quantification (LOQ)µg/mL	0.12687

[a]Regression equation Y=a+bC , Where Y stands for absorbance and C is concentration in µg/mL [b]% Relative standard deviation is calculated for ten determination.

The proposed method has been used for the analysis of teneligliptin.The result obtained are comparable with stanadard method[5] (Table- 2).

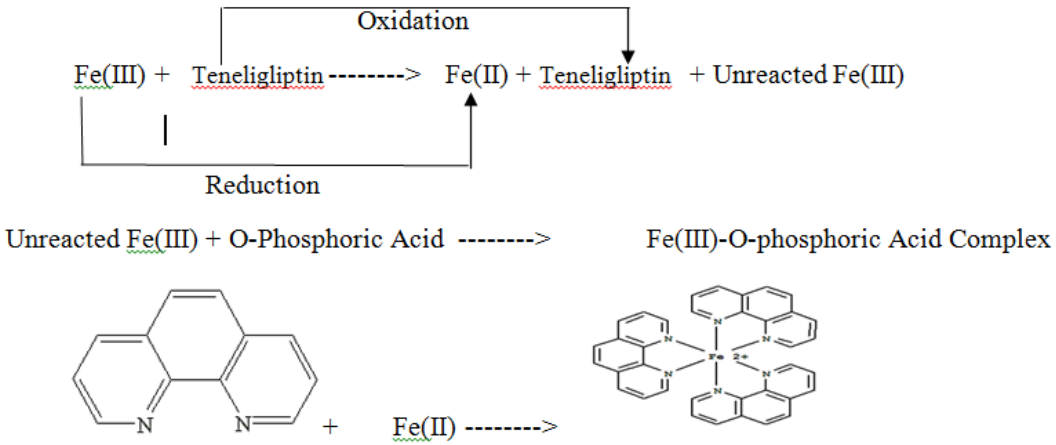
Table-2: Analysis of Pharmaceutical Formulations of Teneligliptin

Drug	Manufacturing company	Labelled amount(mg)	*Amount found by Proposed Method(mg)	*Amount found by Referrence Method(mg)
Teneligliptin	Teneglyn Marketed formulation	20	19.988	19.991

* Average of three determinations

Scheme of coloured product

Ferric salt converts into a ferrous salt upon oxidation and can be easily detected by the usual reagent o-phenanthroline. The reduction product is tris complex of Fe (II), well known as ferroin. The colored prodct of the reaction is given below



CONCLUSIONS

The developed method is simple, sensitive, accurate and reproducible. This method can be successfully applied for the analysis of pharmaceutical formulations in any laboratory.

ACKNOWLEDGEMENTS

The authors are thankful to Principal VES College of Arts Science and commerce, Chembur for providing laboratory facilities.

REFERENCES

1. 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 ObesMetab. 2012 Nov; 14(11): 1040-6.
2. 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.
3. Fukuda-Tsuru S, Anabuki J, Abe Y et al. A novel, potent, and long-lasting dipeptidyl peptidase-4 inhibitor, teneligliptin, improves postprandial hyperglycemia and dyslipidemia after single and repeated administrations. Eur J Pharmacol. 2012 Sep 26. pii: S0014-2999(12)00798-4. doi: 10.1016/j.ejphar.2012.09.024.
4. Kishimoto M et al, DOI: http://dx.doi.org/10.2147/DMSO.S35682,Published Date May 2013 Volume 2013:6: 187 – 195.
5. Bhimireddy Rama Chandra Sekhar Reddy, Nallagatla Vijaya Bhaskar Rao, K. Saraswathi International Journal of Advances in Pharmaceutical Research June 2014; 5(6): 310– 318
6. Aitha Vijaya Laxshmi Asian Journal of Pharmaceutical and Clinical Research 5th January 2013.
7. A. Bisham Babu, G.R AMU, S. Venkata RAO, T. Neeharika and C. Rambabu RASAYAN J. Chem. 2011; 4(2): 336-342.