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Research Article

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Quantitative Determination and Validation of Teneligliptine Hydrobromide Hydrate using FTIR Spectroscopy

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ABSTRACT

A simple, inexpensive and non-destructive strategy was applied for quantitative analysis of teneligliptine hydrobromide hydrate by using transmission Fourier Transform Infrared (FTIR) spectroscopy for routine quality control testing. For the analysis of active pharmaceutical ingredients (API), KBr pellets were prepared having known amount of standards and samples. A procedure for FTIR spectroscopy was developed and validated. The developed method was linear with concentration range of 8 – 14 mg with the adequate precision and recoveries. The intensity (absorbance) at wave numbers of 1263 cm^{-1} and 3454 cm^{-1} were selected for optimization and validation of method. Validation parameters like Linearity, LOD, LOQ, Accuracy and Precision were performed. The regression coefficient (r^2) 0.992 and 0.997 were achieved for teneligliptine hydrobromide hydrate at wave numbers of 1263 cm^{-1} and 3454 cm^{-1} respectively. The above method precisely shows the ability of FTIR spectroscopy for measurement of precise quantity of API to control the quality of finished drug formulation.

Keywords: Transmission FTIR quantitative analysis; Teneligliptine hydrobromide hydrate; IR method validation

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INTRODUCTION

Teneligliptine hydrobromide hydrate is used as an oral anti diabetic agent in type 2 diabetes. Teneligliptine hydrobromide hydrate is DPP-4 inhibitor which lowers the blood glucose level [1]. The analysis of Teneligliptine hydrobromide hydrate either individually or in binary mixture has been usually and routinely carried out by spectrophotometry. All these methods require long procedures and different amount of the organic solvents which contributes toward high analytical cost and generate waste material. FTIR spectroscopy is one of the simple, non-destructive and rapid methods which play a vital role for the fast determination of any ingredients present in matrices of various compounds. FTIR Spectroscopy was widely used for qualitative as well as quantitative analysis of drug [2]. This work based on rapid, solvent free, less expensive and environment friendly method which has been described for quantitative determination of drug by FTIR in multicomponent drug formulations for routine quality control testing. The FTIR method uses unique approach for determining real sample with formation of sample of different concentration. It needs only grinding of sample with KBr for pellet formation [3-10].

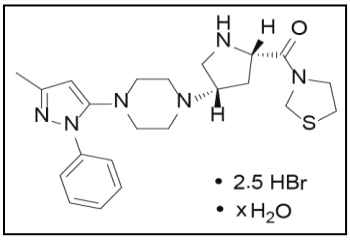

Figure 1: Chemical Structure of teneligliptine hydrobromide hydrate

MATERIALS AND METHODS

FT-IR spectrum for pure drug was taken by FT-IR spectrophotometer using the KBr disk method (Bruker, Germany). The sample was grinded and dispersed with micronized IR grade KBr powder followed by application of 7-12 kpa pressure in the hydraulic KBr press to prepare the disc. The disc was then subjected for FT-IR analysis and comparison was done with the standard spectrum [11,12].

EXPERIMENTAL SECTION

Standards and Samples

Teneligliptine hydrobromide hydrate standard (Assay 99.9%) used to establish calibration was received as gift sample from Glenmark Pharmaceuticals Ltd., Mumbai. KBr used to formulate a standard and sample pellet was IR spectroscopic grade.

FT-IR Spectral Features

FT-IR spectrometer, Bruker, Germany (Model:ALPHA) set with removable KBr optics was used for recording IR spectra of standards and samples of Teneligliptine hydrobromide hydrate. All spectra were obtain in Mid IR region (4000 - 400 cm^{-1}) at a resolution of 8 cm^{-1} collecting 32 scans per spectrum [13-15]. The baseline spectrum of KBr pellet was taken every time before recording standard as well as sample spectra under the same instrumental conditions.

Selection of Wavenumber

Wavenumber selection is depending upon the functional group present in the structure of teneligliptine hydrobromide hydrate. Peak at wavenumbers 3454 cm^{-1} and 1263 cm^{-1} were selected which represents -NH stretching and -CN stretching respectively [16-20]. The linear increase in peak height with increase in concentration confirms that it follows Beer's-Lambert law.

Sample Preparation Procedure

In this method except grinding, there was no prior sample treatment is required for recording FT-IR spectra. The samples were accurately weighed and grinded in mortar until fine powder was obtained. The drug samples in range of 8-14 mg added (Table 1) in KBr to prepare pellets, then mixed in order to homogenize the mixture [21-25]. Afterwards, the pellets were pressed in die at a pressure of 5-8 tons for 2 min. The pellets were made to 250 mg and equal pressure was applied every time to ensure the homogeneity. These pellets were scanned from 4000 to 400 cm^{-1} by using FTIR to record spectra.

Table 1: Composition of KBr pellet with API

Amount of Teneligliptine-hydrobromide hydrate (mg)	Amount of KBr (mg)	Total weight of pellet (mg)
8	242	250
10	240	250
12	238	250
14	236	250

Limit of Detection and Limit of Quantification

Limit of Detection (LOD):

The Limit of Detection was determined from calibration curves by using given formula:

$$LOD=3.3(STDV/Slope)$$

Where, STDV = Standard deviation of the Y- intercepts of the 5 calibration curves, Slope= Mean slope of the 5 calibration curves.

Limit of Quantification (LOQ):

The Limit of Quantification was determined from the set of 5 calibration curves by using given formula:

$$LOQ= 10 (STDV/Slope)$$

Where, STDV= Standard deviation of the Y- intercepts of the 5 calibration curves, Slope= Mean slope of the 5 calibration curves

Accuracy by Recovery and Method Validation

The recovery studies were performed by standard addition method to ensure the accurate results in routine quality control testing [26,27]. In this study, different concentrations of standards i.e. (5, 10, 15 mg) were added to a sample with known concentration and then the total concentration was determined using the proposed method. The recovery efficiency (RE) was estimated using following formula:

RE (%) = (C – B/A) ×100

Where, RE= amount of API recovered (%); B=actual concentration of sample before addition; C=concentration of active pharmaceutical ingredient after addition; A=amount of standard added to sample.

RESULTS AND DISCUSSION

Optimization and Validation of FTIR Spectra

The advantage of this method brings about significant merits in terms of ease, speed and cost by using FTIR spectroscopy for calculating the amount of desired active ingredient during quality control testing of finished pharmaceuticals. Figure 1 shows the FTIR spectra in transmittance mode. Figure 2 illustrates the group FTIR spectrum of API standards in proportionate concentration used for calibration. In this method absorbance mode of FTIR is preferred because of two main difficulties related with transmittance mode. That is sensitivity in comparison to absorbance mode and development of accurate calibration curve. Therefore, absorbance FTIR is excellent choice for accurate determination of active ingredient without using any solvent (Figures 3 and 4).

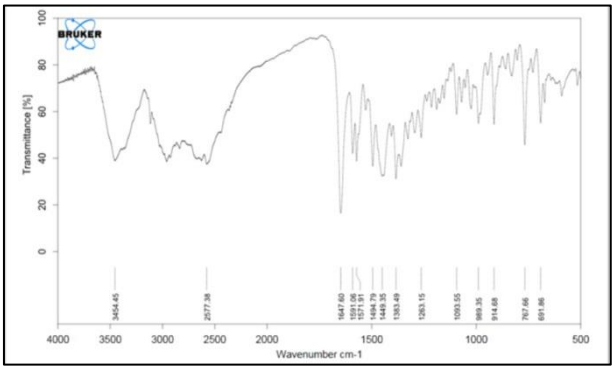

Figure 2: Transmittance FTIR spectra of teneligliptinehydrobromide hydrate scanned overwavenumbers of 4000 - 650 cm^{-1}

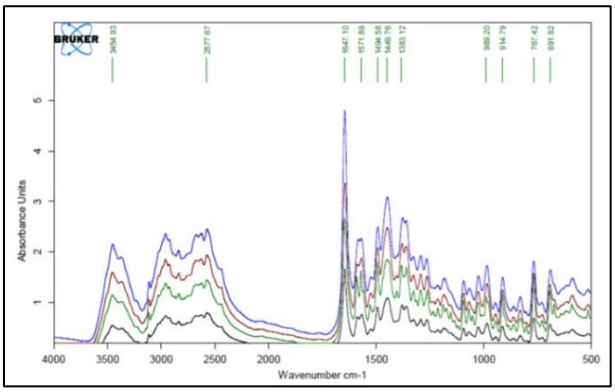

Figure 3: Group FTIR spectra of teneligliptinehydrobromide hydrate scanned over wavenumbers of 4000 - 650 cm^{-1} in Absorbance mode

Method Validation

The method validation and the accuracy of the proposed method were measured by checking recovery efficiency (Tables 2-7). The recovery efficiency was checked by standard addition method on one pre-analyzed selected sample. The results of the standard addition method presented in Table 8 were found to be accurate and precise. The accuracy by recovery values (98.70% to 101.20%) with negligible standard deviation proves that the method is feasible for routine analysis in pharmaceutical laboratories (Figure 5). Moreover, every time fresh amounts were taken to get rid of errors. Table 8 indicates recovery results which are satisfactory.

Linearity

The linear range of API was found to be in the range of 8-14 mg (Figure 2). Calibration curve was constructed by plotting absorbance against concentration. The r^2 values obtained for API were 0.992 and 0.997 at 1263 cm^{-1} and 3454 cm^{-1} respectively.

Table 2: Linearity data of teneligliptine hydrobromide hydrate by FT-IR method

S No.	Concentration (mg)	Absorbance (n=3) At 1263 cm^{-1}	Absorbance (n=3) At 3454 cm^{-1}
1	8	0.99	0.5
2	10	1.357	1.1
3	12	1.643	1.6
4	14	1.897	2.1

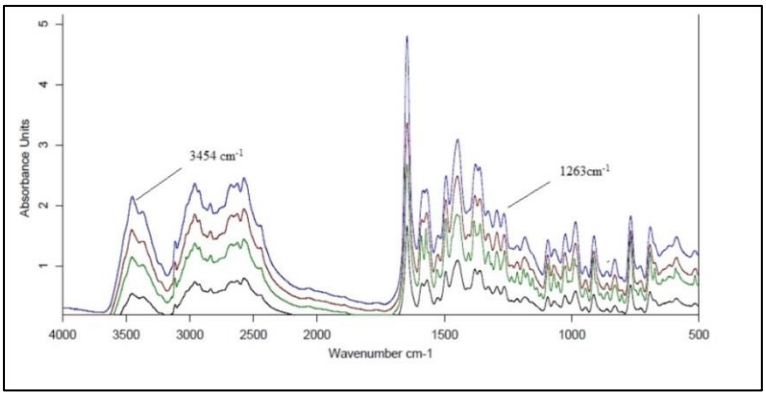

Figure 4: Group FTIR spectra of teneligliptine hydrobromide hydrate showing in absorbance mode

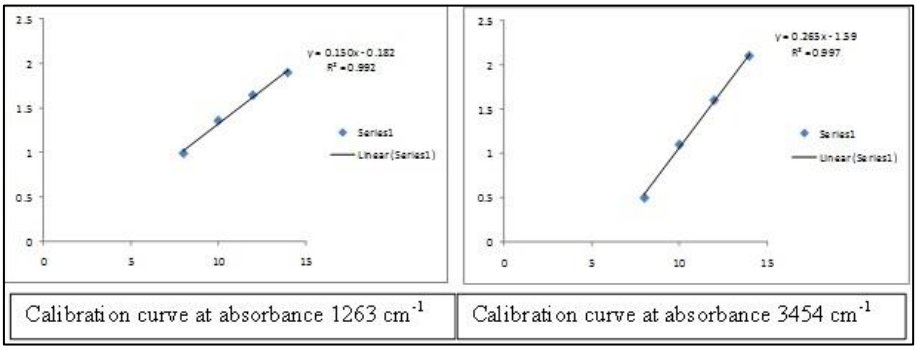

Figure 5: Variation in calibration curves with changing absorbance value

Precision

Repeatability:

The % RSD for repeatability was found to be 0.360 as per absorbance which was within the standard criteria.

Table 3: Intraday precision study data of teneligliptinehydrobromide hydrate at concentration of 10 mg at 1263 cm^{-1}

S No.	1	2	3	4	5	6	Mean	SD	%RSD
Absorbance	0.98	0.971	0.978	0.98	0.979	0.98	0.978	0.004	0.36

Interday:

Interday precision study data.

Table 4: Interday precision study data of teneligliptine hydrobromide hydrate at 1263 cm^{-1}

Parameter	API Conc. (mg)	Day 1	Day 2	Mean	Standard Deviation	% RSD
Absorbance	8	0.98	0.97	0.98	0.007	0.725
	10	1.346	1.344	1.35	0.001	0.105
	12	1.639	1.629	1.63	0.007	0.433
	14	1.892	1.882	1.89	0.007	0.375

Different analyst:

The validity of the proposed method was determined with known concentration of teneligliptine hydrobromide hydrate by two analysts to confirm the precision of method. The % RSD was found to be 0.172-0.718 at 1263 cm^{-1} and 0.646 and 1.4 at 3454 cm^{-1} as per absorbance which confirms the precision of method.

Table 5: Different analyst study data of teneligliptine hydrobromide hydrate at 1263 cm^{-1}

Parameter	API Conc. (mg)	Analyst 1	Analyst 2	Mean	Standard Deviation	% RSD
Absorbance	8	0.99	0.98	0.99	0.007	0.718
	10	1.357	1.346	1.35	0.008	0.576
	12	1.643	1.639	1.64	0.003	0.172
	14	1.897	1.892	1.89	0.004	0.187

Table 6: Different analyst study data of teneligliptinehydrobromide hydrate at 3454 cm^{-1}

Parameter	API Conc. (mg)	Analyst 1	Analyst 2	Mean	Standard Deviation	% RSD
Absorbance	8	0.51	0.50	0.51	0.007	1.400
	10	1.09	1.10	1.10	0.007	0.646
	12	1.63	1.65	1.64	0.014	0.862
	14	2.12	2.15	2.14	0.021	0.994

LOD and LOQ

The Calibration curves were repeated and standard deviation of intercept was calculated for which LOD and LOQ were calculated as follows:

Table 7: Data of LOD and LOQ

Parameter	At 3454 cm^{-1}
SD of the Y-Intercepts of 5 Calibration curve	1.592
Mean slope of 5 calibration curve	0.0148
LOD	0.0307
LOQ	0.0932

Accuracy by Recovery

Accuracy of method was confirmed by recovery study using marketed formulation at 3 different levels of standard addition. The % Recovery was found to be 99.27 - 99.96% at 1263 cm^{-1}

Table 8: Accuracy by %Recovery data at 1263 cm^{-1}

Parameter	Actual amount (mg)	% of nominal Amount	Spiked amount (mg)	Total amount (mg)	Amount found (mg)	% recovery
Absorbance	10	50	5	15	14.89	99.27
	10	100	10	20	19.72	98.60
	10	150	15	25	24.99	99.96

A simple, inexpensive, and non-destructive strategy was applied for the quantitative estimation of teneligliptine hydrobromide hydrate using FTIR spectroscopy for routine quality control testing. For the determination of the active pharmaceutical ingredients (API), KBr pellets containing known amount of standards and samples were used for acquisition of the FTIR spectra.

A procedure for FTIR spectroscopy has been developed and validated. The developed method was linear over the concentration range of 8-14 mg with the acceptable precision and recoveries. The intensity (absorbance) at wave numbers of 1263 cm^{-1} and 3454 cm^{-1} were selected for optimization and validation of method. Validation parameters like Linearity, LOD, LOQ, Accuracy and Precision were performed. The regression coefficient (r^2) 0.992 and 0.997 were achieved for teneligliptine hydrobromide hydrate at wave numbers of 1263 cm^{-1} and 3454 cm^{-1} respectively. The above method precisely shows the capability of transmission FTIR spectroscopy for assessment of exact quantity of API to control the quality of finished products.

DISCUSSION

The above work shows estimation of teneligliptine hydrobromide hydrate in tablet dosage form by using FTIR spectroscopy for routine quality control testing. The linearity range (8-14 mg) with acceptable precision and recovery was found at wave numbers 1263 cm^{-1} and 3454 cm^{-1} for the method. Precision was determined by studying the interday and intraday precision. The standard deviation and Relative Standard deviation (% RSD) were calculated at both frequencies. For proposed method % RSD were not more than 2.0% which shows good intermediate precision. The values LOD and LOQ were 0.0307 mg and 0.0932 mg at 3454 cm^{-1}. Percentage estimation of API in tablet dosage form was 99.27% and 99.96% by the proposed method.

CONCLUSION

The method for the assessment of teneligliptine hydrobromide hydrate in finished product samples by FTIR is a simple analytical method which is inexpensive and environmental friendly. It removes the complication of usual extraction methods allowing rapid analysis without using any solvent. So it has wide applications in pharmaceutical industry as it is in accordance with the green chemistry needs and fulfils industrial demand of

faster and inexpensive method. The approach of using FTIR for direct determination of API in pharmaceutical formulation where several ingredients are present provides an alternate for the costly and extensive procedures used for quality control testing routinely performed in pharmaceutical industries.

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