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Research Article

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Simultaneous Estimation of Teneligliptin and Metformin Hydrochloride in Tablet Formulation by UV Spectrophotometric Method

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Abstract Simple, sensitive and accurate UV-spectroscopic methods were developed and validated for simultaneous estimation of Teneligliptin and Metformin Hydrochloride in tablet formulation using simultaneous equation method. Wavelengths which could be utilized for simultaneous analysis of TGN and MET were 245 nm (λ_{max} of TGN) and 233 nm (λ_{max} of MET) respectively from the overlain spectra. Linearity was found to be satisfactory over the concentration range of 1-30 µg/ml for both the drugs. The mean percentage label claim of Teneligliptin and Metformin Hydrochloride using Simultaneous equation method was found to be 99.46% of teneligliptin and 99.49% of metformin hydrochloride and respective values of standard deviation were 1.09 for teneligliptin and 0.50 for metformin hydrochloride. Percentage recovery was found in the range of 98.29 - 101.80% for teneligliptin and 99.20 - 99.90% for metformin hydrochloride. The developed method is economical and reproducible for routine analysis of Teneligliptin and Metformin Hydrochloride in tablet formulation.

Keywords Teneligliptin, Metformin Hydrochloride; Simultaneous equation Method; Validation, tablet formulation

Introduction

Chemically Teneligliptin hydrobromide is {(2s,4s)-4-[4-(3-Methyl-1-phenyl-1*H*-pyrazole-5-yl) piperazin-1-yl] pyrrolidin-2-yl} (1, 3-thiazolidin-3-yl) methanone hemipenta hydrobromide hydrate. Teneligliptin hydrobromide hydrate is a white to light tan solid. It is highly potent, competitive and long-lasting dipetidyl peptidase-4 (DPP-4) inhibitors that improve postprandial hyperglycaemia and dyslipidemia. Teneligliptin drug inhibit the enzyme DPP-4 which degrades incretin, a hormone adjusting blood glucose level [1-5].

Metformin hydrochloride is chemically 3-(diaminomethylidene)-1,1-dimethyl-guanidine; hydrochloride It is a white to off-white crystalline compound. It can be stored at room temperature. Metformin hydrochloride is an oral anti-hyperglycemic drug used in the management of type 2 diabetes. Metformin hydrochloride (biguanide hypoglycemic agent) is not chemically or pharmacologically related to any other classes of oral antihyperglycemic agents [6-9].

Several analytical methods have been reported for estimation of Teneligliptin [10-11] and its combination with other drugs [12-13] which includes spectrophotometry and HPLC. Similarly, various spectrophotometric and HPLC methods have been reported for estimation of Metformin hydrochloride and its combination with other drugs [14-15]. In the present work, a successful attempt has been made to estimate both these drugs simultaneously using UV spectrophotometric method.

Materials and Methods

Instrumentation

A double beam UV spectrophotometer (UV-1800, Shimadzu, Japan) with UV probe software version (2.31) and 10mm quartz cells was used. All weights were taken on an electronic balance (Schimadzu - 220h).

Reagents and Chemicals

Pure drug, Teneligliptin Hydrobromide Hydrate and Metformin Hydrochloride was procured from Molecule laboratory, Ahmedabad, India. Marketed formulation was procured from local Pharmacy. All the chemicals and reagents used were of A.R. grade.

Method Development

Preparation of standard stock solution

The standard stock solutions of Teneligliptin Hydrobromide Hydrate and Metformin Hydrochloride were prepared by dissolving 147.41 mg of Teneligliptin Hydrobromide Hydrate (147.41 mg of Teneligliptin Hydrobromide Hydrate is equivalent to 100 mg of Teneligliptin) and by dissolving 100 mg of MET in separate 100 mL volumetric flask containing sufficient quantity of distilled water, it was vortexed for 5 min then volume was made up to the mark with distilled water to get a concentration of 1000 µg/mL. 5 ml from each solution was transferred in two separate 50 ml volumetric flask and diluted with distilled water to obtain working standard solution of 100 µg/mL. The standard stock solutions were further diluted to obtain desired concentrations.

Preparation of sample solution

Twenty tablets were weighed and powdered. The quantity of the powder equivalent to 20 mg of TGN was transferred into 100 ml volumetric flask then 250 mg of standard drug of MET was added in same volumetric flask. The content was mixed with sufficient quantity of distilled water and sonicated for 20 min to dissolve the drug. The solution was then filtered through a Whatman filter paper no. 41, filter paper was washed with diluents and the washings were added into the same volumetric flask. The volume was made up to the mark with distilled water, mixed well to get a concentration of 400 µg/mL of TGN and 5000 µg/mL of MET in sample stock solution. An aliquot of solution (2.5 ml) was transferred into a 50 ml volumetric flask and the volume was adjusted up to the mark with distilled water to obtain required concentration of 20 µg/ml of TGN and 250 µg/ml of MET. Further 1 mL of the above solution was diluted upto 10 mL to obtain required concentration of 2 µg/ml of TGN and 25 µg/ml of MET.

Simultaneous Equation method

For simultaneous estimation of TGN and MET using simultaneous equation method (SE method) the solutions of TGN (2 µg/ml) and MET (25 µg/ml) were prepared from the standard stock solutions of TGN and MET and scanned over the range of 200 nm to 400 nm. An overlain spectrum was studied for development of suitable method for analysis. The overlain spectrum of TGN and MET is shown in (Figure 1). From the overlay spectra, 245 nm (λ_{max} of TGN) and 233 nm (λ_{max} of MET) were selected for the estimation of TGN and MET using simultaneous equation method. The absorptivity values were calculated and were applied in framed simultaneous equation 1 and 2, which is presented as,

$$C_{TGN} = \frac{0.0391A_2 - 0.0723A_1}{-0.00095} \quad \textbf{…Eqn. 1} \qquad C_{MET} = \frac{0.0233A_1 - 0.0257A_2}{-0.00095} \quad \textbf{…Eqn. 2}$$

where A_1 and A_2 = absorbance of the solution at 245nm and 233nm respectively, C_{TGN} and C_{MET} are concentrations of TGN and MET, respectively in µg/ml.

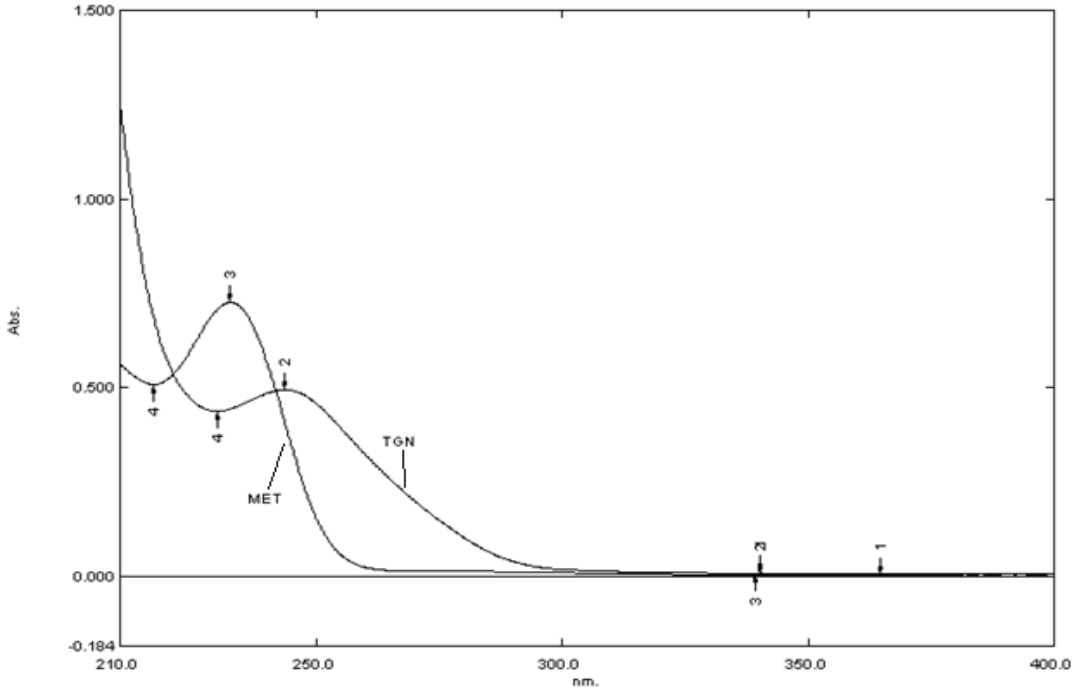

Figure 1: Overlain spectra of teneligliptin and metformin hydrochloride

Analysis of ALS & AML in tablet formulation

The absorbance values of final sample solution were measured against distilled water as blank at 245 nm and 233 nm for quantitation of TGN and MET, respectively. The amount of TGN and MET present in the sample solutions were determined by solving the above framed simultaneous equations (SE) 1 and 2. The analysis procedure was repeated five times for marketed formulation.

Method Validation

Linearity and Range

Aliquots of standard solution of TGN and MET (0.1, 0.5, 1.0, 2.0 and 3.0 ml) were transferred in a series of 10 ml volumetric flasks. The volume was adjusted up to the mark with distilled water and mixed. Absorbance values were recorded at 245 nm and 233nm for SE method against distilled water as blank. The calibration curves were plotted between the concentration of component and absorbance values of TGN and MET for SE method

Standardization of the method by analysis of mixed standard solutions

To check the validity of this method, mixed standard solutions of TGN and MET were prepared. The solutions were subjected to determine absorbance values at respective wavelengths and concentration of the components were calculated.

Accuracy

The accuracy of the method was determined for both the methods by calculating recoveries of TGN and MET by the standard addition method. Known amount of standard solution of TGN and MET were added at 80%, 100% and 120% levels to pre-quantified tablet sample solutions of TGN and MET. The results are reported in terms of % Recovery.

Results and Discussion

Method development and validation

A simple, sensitive and accurate UV-spectroscopic methods ws developed and validated for simultaneous estimation of teneligliptin and metformin hydrochloride in tablet formulation using Simultaneous equation spectroscopic method. From the overlain spectra of the drugs it was observed that SE spectroscopic method was suitable method for simultaneous determination of TGN and MET. Distilled water was taken as solvent system, as both the drugs were soluble in this solvent and reduce the cost of the method. In SE method, wavelengths 245 nm and 233 nm respectively were selected for determination of TGN and MET respectively, Optimized method parameters for simultaneous equation spectroscopic methods are shown in (Table 1).

Table 1: Optimized method parameters for simultaneous equation method

Method	SE Method
Solvent	Distilled water
Scanning range	210-400 nm
Analytical wavelength for determination of TGN	245 nm
Analytical wavelength for determination of MET	233 nm
Linearity range for ALS	1-30 µg/ml
Linearity range for AML	1-30 µg/ml

Standardization of the method by analysis of mixed standard solutions

The concentration of TGN and MET recovered from mixed standard solutions for both methods was within range and are given in (Table 2).

Table 2: Results of validation studies of teneligliptin and metformin hydrochloride by simultaneous equation method using mixed standards

S. No.	Amount Present (µg/ml)		Amount Found (µg/ml)		%	
	TGN	MET	TGN	MET	TGN	MET
1	5	25	5.02	24.88	100.50	99.52
2	10	20	10.03	19.85	100.31	99.26
3	15	15	15.06	15.06	100.38	100.43
4	20	10	20.04	9.97	100.21	99.73
5	25	5	25.14	5.01	100.56	100.20

Accuracy

The percentage recoveries of drugs from sample were determined by standard addition of pure drugs at three known concentrations and recoveries were obtained at each level. The percent recoveries for TGN was found to be in the range of 99.67- 100.69% and for MET was found to be in the range of 99.20-99.66%. The results of accuracy studies are shown in (Table 3).

Table 3: Accuracy study for teneligliptin and metformin hydrochloride by simultaneous equation method

Accuracy Level (%)	Amount Added (µg/ml)		Amount Recovered (µg/ml)		% Recovery		Mean	
	TGN	MET	TGN	MET	TGN	MET	TGN	MET
80	0.8	10	0.81	9.92	100.64	99.20	100.64	99.20
	0.8	10	0.81	9.89	101.42	99.90		
	0.8	10	0.80	9.95	99.86	99.49		
100	1.0	12.5	0.99	12.43	98.92	99.46	99.67	99.63
	1.0	12.5	0.98	12.46	98.29	99.70		
	1.0	12.5	1.02	12.47	101.80	99.72		
120	1.2	15	1.20	14.98	100.17	99.86	100.69	99.66
	1.2	15	1.21	14.92	101.21	99.46		
	1.2	15	1.21	14.95	100.69	99.66		

Application of the method in assay of tablets

The proposed UV method was applied for the determination of TGN and MET in their combined pharmaceutical formulation and the results are shown in (Table 4).

Table 4: Analysis of formulation of teneligliptin and metformin hydrochloride by simultaneous equation method

Sample No.	Label Claim (mg/tab)		Amount Found (mg/tab)		% Label Claim	
	TGN	MET	TGN	MET	TGN	MET
1	20	500	19.83	495.05	99.15	99.01
2	20	500	19.66	499.25	98.29	99.85
3	20	500	20.24	499.90	101.18	99.97
4	20	500	19.95	494.45	99.77	98.89
5	20	500	19.78	499.66	98.92	98.73
		Mean			99.46	99.49
		S.D.			1.09	0.50
		% RSD			1.10	0.51

*Mean ± SD (n=5), SD (Standard deviation), % RSD (Percent relative standard deviation)

Conclusion

The proposed simultaneous equation method gives accurate and precise results for determination of teneligliptin and metformin hydrochloride in marketed formulation (tablet) without prior separation and is easily applied for routine analysis. Method validation has been demonstrated by variety of tests like linearity, accuracy, precision and validation through mixed standard. The proposed method can be successfully applied for determination of these drugs in commercial tablet formultion.

Conflict interests

The authors declare that there is no conflict of interest.

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