WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 5, 1494-1505. Research Article ISSN 2277– 7105

DUAL WAVELENGTH SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF BENIDIPINE HYDROCHLORIDE AND TELMISARTAN IN PHARMACEUTICAL DOSAGE FORM

Khyati Patel*, Darshil Shah and Dr. Dilip Maheshwari

L.J. Institute of Pharmacy, Nr. Sanand Cross Roads, Sarkhej-Gandhinagar Highway, Ahmedabad Gujarat-382210, India.

Article Received on
15 Jan. 2018,

Revised on 07 Feb. 2018,
Accepted on 27 Feb. 2018,

DOI: 10.20959/wjpr20185-10878

***Corresponding Author**
Khyati Patel
L.J. Institute of Pharmacy, Nr. Sanand Cross Roads, Sarkhej-Gandhinagar Highway, Ahmedabad Gujarat-382210, India.

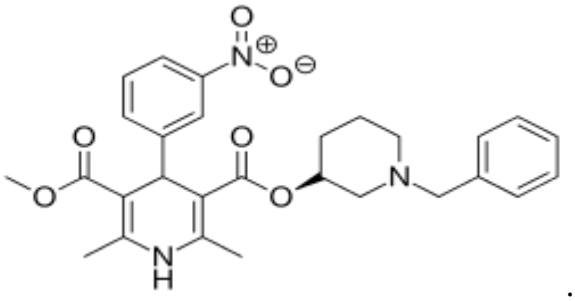
ABSTRACT

The present manuscript describes simple, sensitive, rapid, accurate, precise and cost effective dual wavelength spectrophotometric method for the simultaneous determination of Benidipine HCl(BEN) and Telmisartan(TEL) in combined tablet dosage form. The utility of dual wavelength data processing program is its ability to calculate unknown concentration of components of interest in a mixture containing an interfering component. The principle for dual wavelength method is —the absorbance difference between two points on the mixture spectra is directly proportional to the concentration of the component of interest. The method was based on determination of Benidipine HCl at the absorbance difference between 228.36nm and 245.39nm and Telmisartan at the absorbance difference between 280.21 nm and 315.39 nm. The linearity was obtained in the concentration range of 1-5 µg/ml for Benidipine HCl and 10-50 µg/ml for Telmisartan. The accuracy and precision of the method was determined and validated statically. The method showed good reproducibility and recovery with % RSD less than 2. Method was found to be rapid, specific, precise and accurate, can be successfully applied for the routine analysis of Benidipine HCl and Telmisartan in bulk, and combined dosage form without any interference by the excipients. The method was validated according to ICH guidelines.

KEYWORDS: Benidipine HCl(BEN) and Telmisartan(TEL).

INTRODUCTION[1-6]

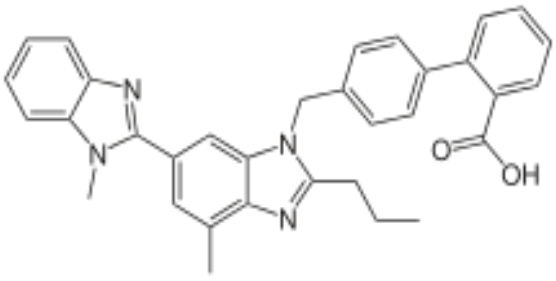
Benidipine Hydrochloride is a dihydropyridine calcium channel blocker. It is also commonly used for the small subset of pulmonary hypertension patients whose symptoms respond to calcium channel blockers. Also used in the long term treatment of hypertension and angina pectoris. The chemical name of the Benidipine HCl is 3-(3R)-1-benzylpiperidin-3-yl 5-methyl (4R)-2, 6-dimethyl-4-(3-nitrophenyl)-1, 4-dihydropyridine-3, 5-dicarboxylate hydrochloride.



HCl

Structure of Benidipine HCl

Telmisartan is an anginotensin 2 receptor antagonist. That is selective for the type 1 anginotensin receptor. It is used to treat high blood pressure, congestive heart failure and to reduce death for people with left ventricular dysfunction after having had a heart attack. The chemical name of the Telmisaratn is 2-(4-{[4-Methyl-6-(1-methyl-1H-1,3-benzodiazol-2-yl)-2-propyl-1H-1,3-benzodiazol-1-yl] methyl} phenyl) benzoic acid.



Structure of Telmisartan

Literature survey revealed that Benidipine Hydrochloride can be estimated by spectrophotometry and by liquid chromatographic methods individually or in combination with other drugs, and Telmisartan can be estimated by spectrophotometry and by liquid chromatographic methods individually or in combination with other drugs. Dual wavelength spectrophotometric method is considered to be a good alternative, and it should be widely

explored as an important tool in routine drug analysis. The aim of the present work was to develop an accurate, repeatable, sensitive and specific UV spectrophotometric method for the determination of BEN HCl and TEL in formulation as stipulated by the ICH guidelines. The proposed method was validated according to ICH guidelines and its updated international convention.

MATERIALS AND METHODS[7-9]

Apparatus and instruments

- U.V. visible spectrophotometer: A Shimadzu model 1800 with software UV Probe
- version 2.3.1)
- Digital Analytical Balance – Wensar DA13-220 (INDIA)
- Sonicator- Equitron (India)
- Volumetric flasks: 10, 50 and 100 ml (Borosil)
- Pipettes- 1,2 and 10 ml (Borosil)
- Beakers- (Borosil)

Preparation of standard stock solution (100µg/ml)

Accurately weighed portion BEN HCl and TEL 10 mg was transferred to a 10 ml volumetric flask and dissolved and diluted to the mark with methanol to obtain solution having concentration of BEN HCl and TEL (1000 µg/ml). From this 1 ml was pipetted out in 10 ml volumetric flask and diluted to the mark with methanol to obtain standard stock solution of 100 µg/ml. Selection of analytical wavelength Accurately weighed 10 mg of BEN HCl and 10 mg TEL was transferred into 100 ml volumetric flask, separately and dissolved in small volume of methanol. The volume was adjusted to the mark with methanol to obtain final concentration of BEN HCl and TEL (100 µg/ml). 1 ml of this solution was transferred in 10 ml volumetric flask and volume was adjusted to the mark with methanol, to prepare a final concentration 10 µg/ml. This standard solution of BEN HCl and TEL was scanned in UV range 200-400 nm in 1cm cell against methanol was blank and maximum absorbance was measured for selection of λ max of BEN HCl and TEL. From the overlain spectra, four wavelengths 228.36 nm and 245.39 nm for BEN HCl and 280.21 nm and 315.39 nm for TEL were selected for quantitation of both the drugs by proposed Dual wavelength spectrophotometric method. The quantitative determination of BEN HCl was carried out by measuring the absorbance difference at λmax of 228.36nm and 245.39 nm where TEL shows same absorbance value. The quantitative determination of TEL was carried out by measuring

the absorbance difference at 280.21 nm and 315.39 nm where BEN HCl showed same absorbance value at both the wavelengths.

Calibration curve for BEN HCl and TEL

Appropriate aliquot of stock solution was taken in five different 10 ml volumetric flask. Volume was made up to the mark with methanol to obtain final concentration of 1-5 µg/ml of BEN HCl and 10-50 µg/ml of TEL respectively. The responses of the sample solution were measured at 228.36 nm and 245.39 nm for BEN HCl and 280.21 nm and 315.39 nm for TEL respectively. The amount of BEN HCl and TEL present in the sample solution were determined by substituting the absorbance into the regression equation for BEN HCl and TEL respectively.

Validation[10-12]

- The developed method was validated with respect to linearity, accuracy, intraday and interday precision, LOD and LOQ in accordance with the ICH guideline.

- **Linearity and range**

Linearity was studied by preparing standard solutions at 5 different concentrations. The linearity range for BEN HCl and TEL were found to be 1-5 µg/ml and 10-50 µg/ml respectively. Linearity was assessed in the terms of slope, intercept and correlation coefficient for both the drugs.

- **Precision**

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision may be considered at 3 levels: Repeatability, intermediate (intraday) precision and reproducibility (interday) precision.

1. **Intraday precision**

Solutions containing 2,3,4 µg/ml for BEN HCl and 20,30,40 µg/ml for TEL were analysed 3 times on the same day and % RSD was calculated.

2. Interday precision

Solutions containing 2,3,4 µg/ml for BEN HCl and 20,30,40 µg/ml for TEL were analysed 3 times on the different successive days and % RSD was calculated.

3. Repeatability

Method precision of experiment was performed by preparing the standard solutions of BEN HCl 3 µg/ml and TEL 30 µg/ml for six times and analysed as per the proposed method. % RSD was NMT 2%.

- **Limit of detection (LOD)**

Limit of detection can be calculated using following equation as per ICH guidelines.

LOD = 3.3 x (σ/S)

Where, σ = the standard deviation of the response

S = the slope of the calibration curve

- **Limit of quantification (LOQ)**

Limit of quantification can be calculated using following equation as per ICH guidelines.

LOQ = 10 x (σ/S)

Where, σ = the standard deviation of the response

S = the slope of the calibration curve

- **Accuracy**

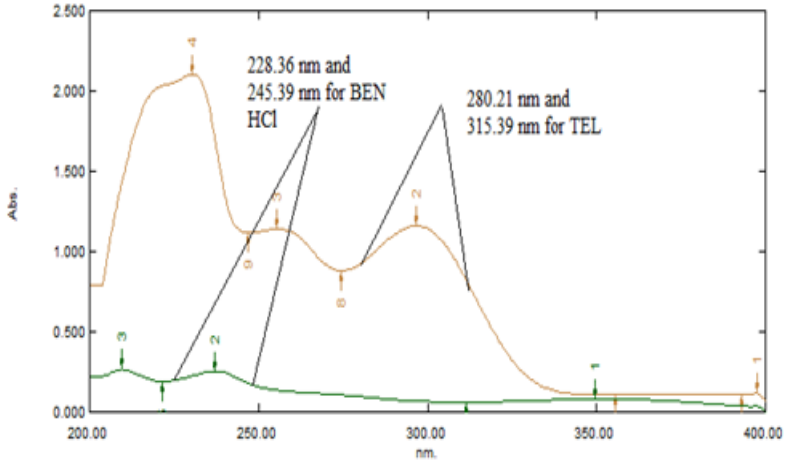
Accuracy expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. Recovery studies were carried out by addition of standard drug to the sample at 3 different concentration levels (80%, 100%, 120%) taking into consideration percentage recovery of added bulk drug samples. The experiment was repeated three times by spiking previously analysed samples of tablet with three different concentration of standards.

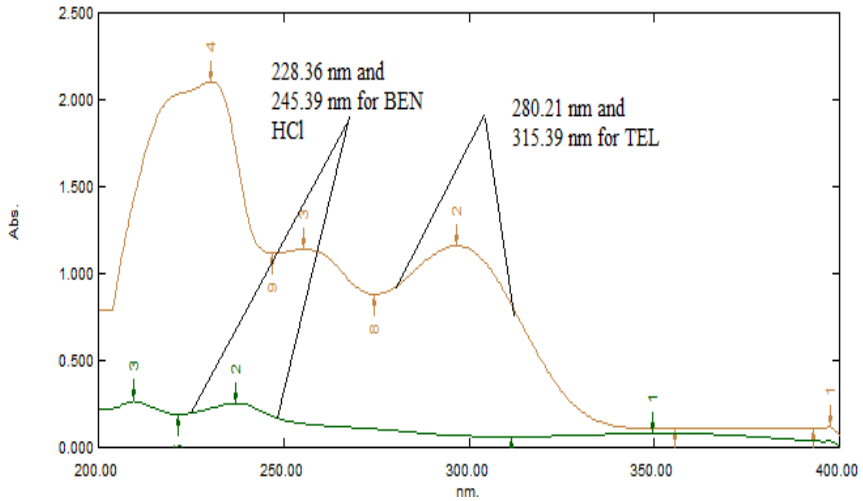
RESULT AND DISCUSSION

Selection of wavelength for simultaneous estimation of BEN HCl and TEL

To determine the wavelength for measurement, BEN HCl (4 µg/ml) and TEL (40µg/ml) solutions were scanned between 400-200 nm. Absorbance difference were obtained their ƛmax 228.36 nm and 245.39 nm for BEN HCl and 280.21 nm and 315.39 nm for TEL respectively.

Overlain spectra of BEN HCl (4 µg/ml) and TEL (40 µg/ml)

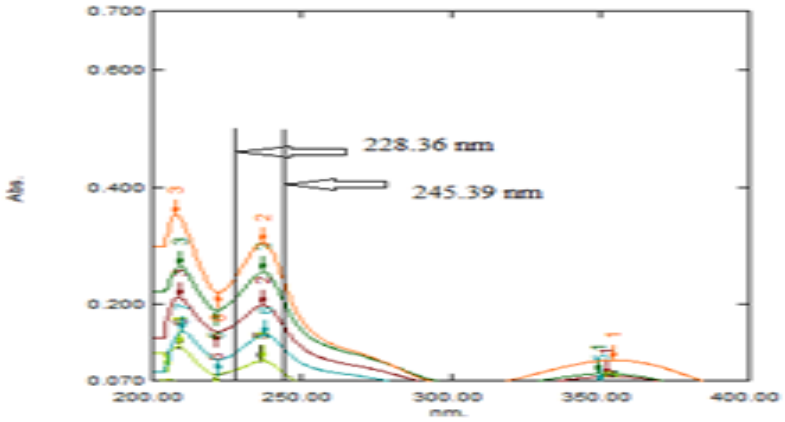


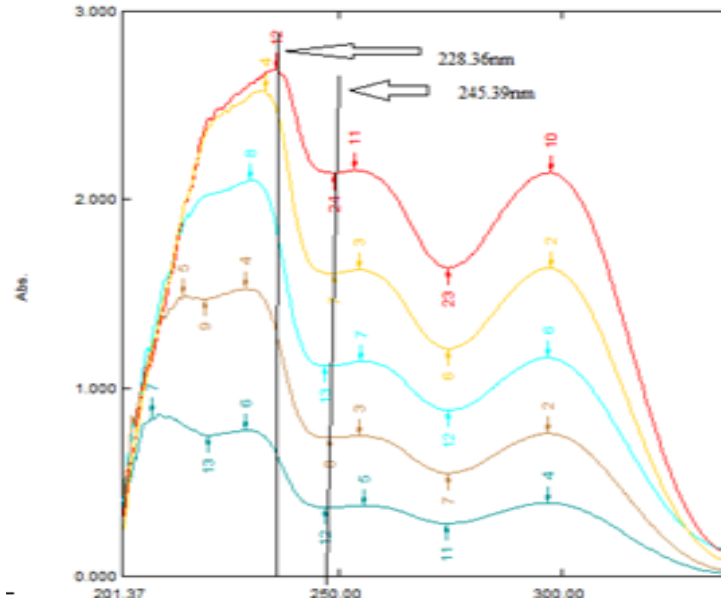


Method validation

Linearity and range

The linearity of BEN HCl and TEL was found to be in the range of 1-5 µg/ml and 10-50 µg/ml respectively.

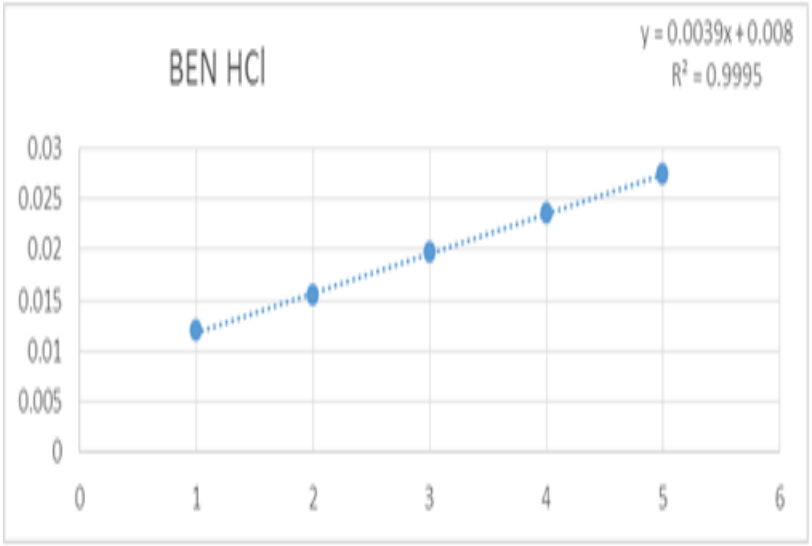


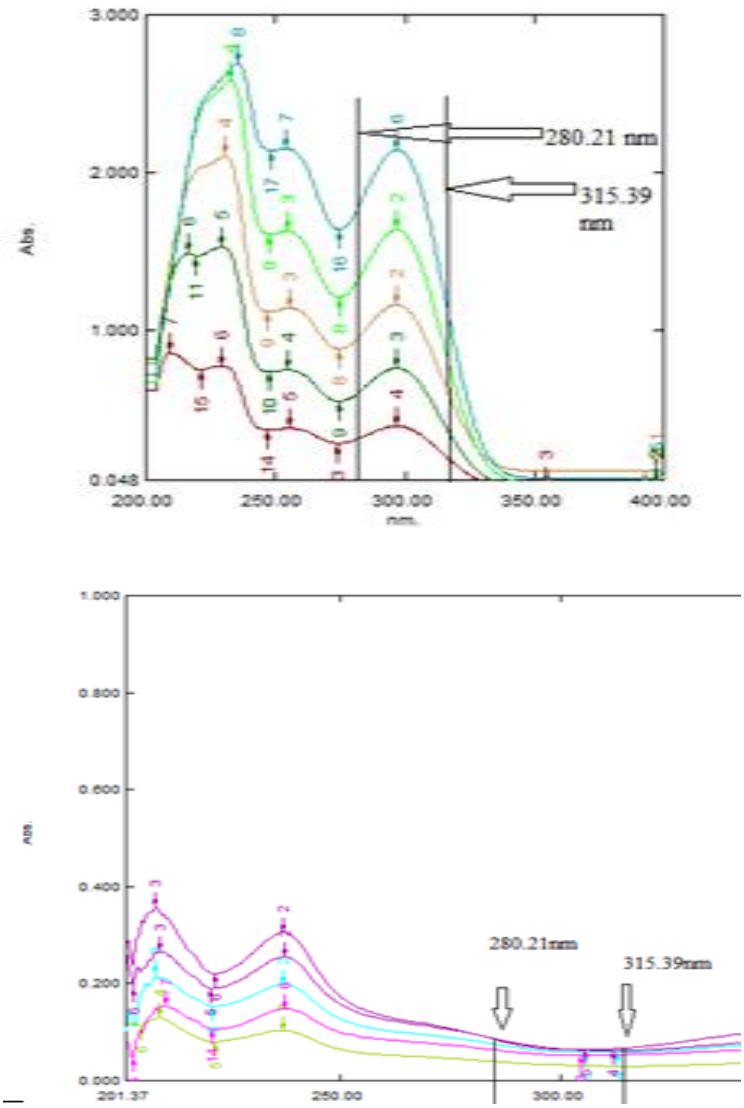


Spectra of Benidipine HCl and Telmisartan for different conc. At 228.36 nm and 245.39 nm where BEN HCl has same absorbance and TEL has different absorbance.

Linearity of Benidipine HCl

Conc (µg/ml)	Mean	S.D	%R.S.D
1	0.01233	0.00021	1.75
2	0.0155	0.000261	1.68
3	0.01951	0.000264	1.35
4	0.02345	0.000288	1.22
5	0.000331	0.000331	1.20

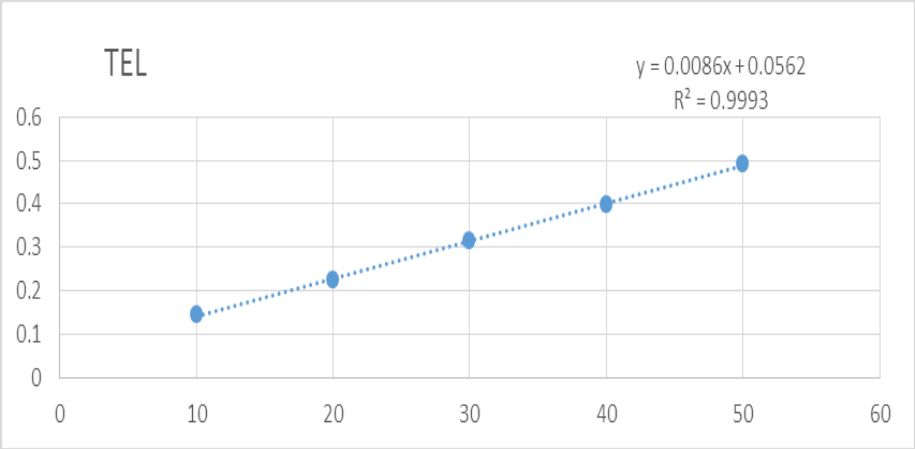




Spectra of TEL and BEN HCl for different conc. At 280.21nm and 315.39 nm where TEL has same absorbance and BEN HCl has different absorbance.

Linearity of Telmisartan

Conc (µg/ml)	Mean	S.D	%R.S.D
10	0.1431	0.002317	1.61
20	0.2245	0.002429	1.08
30	0.3138	0.002639	0.84
40	0.3945	0.002881	0.73
50	0.4948	0.003312	0.66



Precision

1. Intraday Precision

The data for Intraday precision for BEN HCl and TEL is in range of % RSD was found to be 1.6 - 1.3% for BEN HCl at 228.36 nm – 245.39 nm and 1.5 – 0.8 for TEL at 280.21 nm – 315.39 nm.

Precision data for Benidipine HCl and Telmisartan

Drug	conc. (µg/ml)	Absorbance mean ± S.D (N=3)	%R.S.D
Benidipine HCl	2	0.0166 ± 0.000266	1.6
	3	0.0185 ± 0.00029	1.5
	4	0.0232 ± 0.000303	1.3
Telmisartan	20	0.1643 ± 0.0025	1.5
	30	0.2954 ± 0.0032	1.08
	40	0.3948 ± 0.0033	0.8

2. Interday Precision

The data for Interday precision for BEN HCl and TEL is in range of % RSD was found to be 1.74 – 1.46 % for BEN HCl at 228.36 nm – 245.39 nm and 1.63 – 0.98 % for TEL at 280.21 nm – 315.39 nm.

Precision data for Benidipine HCl and Telmisartan

Drug	conc. (µg/ml)	Absorbance mean ± S.D (N=3)	%R.S.D
Benidipine HCl	2	0.0192 ± 0.00033	1.74
	3	0.0214 ± 0.00036	1.68
	4	0.0254 ± 0.00037	1.46
Telmisartan	20	0.196 ± 0.0032	1.63
	30	0.289 ± 0.0035	1.23
	40	0.375 ± 0.0037	0.98

3. Repeatability

The data for repeatability for BEN HCl and TEL is in range of % RSD was found to be 0.7 % for BEN HCl at 228.36 nm – 245.39 nm and 0.9 % for TEL at 280.21 nm – 315.39 nm.

Drug	conc. (µg/ml)	Absorbance mean ± S.D (N=3)	%R.S.D
Benidipine HCl	4	0.0234 ± 0.000264	1.12
Telmisartan	40	0.394 ± 0.002317	0.58

LOD and LOQ

LOD values for BEN HCl and TEL were found to be 0.0255 µg/ml and 0.0212 µg/ml respectively. LOQ values for BEN HCl and TEL were found to be 0.0773 µg/ml and 0.0642 µg/ml respectively.

LOD and LOQ data table

Parameter	Benidipine HCl	Telmisartan
Standard deviation	0.000214	0.002908
Slope	0.003817	0.008733
LOD (µg/ml)	0.184	1.09
LOQ (µg/ml)	0.559	3.33

Accuracy

Accuracy of the method was confirmed by recovery study from marketed formulation at three levels (80%, 100%, 120%). Percentage recovery for BEN HCl and TEL were found be in the range of 99.37-105.55% for both the drug.

Data indicating recovery studies of BEN HCl and TEL are shown in table.

Drug	% level of recovery	Amount of drug taken (µg/ml)	Amount of drug added (µg/ml)	Total amount found (µg/ml)	% recovery
Benidipine HCl	50	2	1	2.95	98.33
	100	2	2	4.05	101.25
	150	2	3	5.02	100.4
Telmisartan	50	20	10	30.45	101.5
	100	20	20	39.75	99.37
	150	20	30	49.75	99.5

Analysis of marketed formulation

Applicability of the proposed method was tested by analysing the commercially available tablet formulation. (INZIT TL 40). It is shown in table.

Tablet	Drug	abel claim	mount found	% bel claim
Inzit TL 40	Benidipine HCl	4 mg	4.05	101.25
	Telmisartan	40 mg	39.2	98

Regression analysis data and summary of validation parameters for the proposed method.

Parameters	BEN HCl	TEL
Wavelength	228.36-245.39 nm	280.21-315.39 nm
Beer's law limit (µg/ml)	1-5	10-50
Regression equation (y = mx + c)	y = 0.0039x + 0.008	y = 0.0086x + 0.0562
Slope (m)	0.0039	0.0086
Intercept (c)	0.008	0.0562
Correlation coefficient (r^2)	0.9995	0.9993
Repeatability (% RSD, n=6)	1.12	0.58
Interday (n=3) (%RSD)	1.74 - 1.46	1.63 – 0.98
Intraday (n=3) (%RSD)	1.6 - 1.3	1.5 – 0.83
LOD (µg/ml)	0.184	1.09
LOQ (µg/ml)	0.559	3.33

CONCLUSION

A simple, accurate and precise spectrophotometric method has been developed and validated for the routine analysis of BEN HCl and TEL in API and tablet dosage form. the spectrophotometric method is suitable for the simultaneous determination of BEN HCl and TEL in multicomponent formulation without interference of each other.

The Dual wavelength method is rapid, simple and sensitive. The developed method is recommended for routine and quality control analysis of the investigated drugs in two components pharmaceutical preparation.

ACKNOWLEDGEMENT

The authors are thankful to Dr. K. Pundarikakshudu, Director of L. J. Institute of Pharmacy, Ahmedabad, India for providing all the facilities and encouragement to carry out the work.

REFERENCES

1. Siyad A.R. Hypertension, H.J.D. Med. April-October 2011; 3(1): 1-16.
2. Wells BG., Dipiro JT., Schwinghammer TJ., and Dipiro CV, Pharmacology Therapy; 7th Edition; The Mcgraw-Hills Companies, 2009; 112.
3. Pubchem, "Benidipine Hydrochloride Drug profile".

https://pubchem.ncbi.nlm.nih.gov/compound/benidipine_hydrochloride.

4. Japanese Pharmacopoeia; The Ministry of Labour, Family and Welfare., 2006; 338-342.
5. Kozo Y, Ken N and Hiroyuki M, "Pharmacological, Pharmacokinetic, and Clinical Properties of Benidipine Hydrochloride, a Novel, Long-Acting Calcium Channel Blocker". *J* PharmacolSci, 2006; 100: 243 – 261.
6. Maryadele J., Heckelman PE., Koch CB., and Roman KJ. The Merck Index Anencyclopedia of chemicals, drugs and biological; 14th Edition; Merck Research Laboratories UK, 2006; 1043.
7. PubChem, "Telmisartan Drug profile". https://pubchem.ncbi.nlm.nih.gov/compound/Telmisartan
8. Maryadele J., Heckelman PE., Koch CB., and Roman KJ. The Merck Index Anencyclopedia of chemicals, drugs and biological; 14th Edition; Merck Research Laboratories UK, 2006; 1129-1569.
9. Indian Pharmacopoeia; Government of India Ministry of Health and Family Welfare Published by Indian Pharmacopoeia Commission, Ghaziabad, 2014; 2: 1893-1894, 2830-2832, 2336-2340.
10. Swartz ME. And Krull IS. Analytical method Development and validation; Boston (USA), 1997; 25-46.
11. Skoog DA, Hollar JA, Nieman TA, Principle of Instrumental Analysis; 5thEdn; Thomsan Asia Pvt. Ltd, 300-328, 725-744.
12. Owen T. Fundamentals of UV-visible Spectroscopy; Hewlett-Packard publication, 38-45.