RESEARCH ARTICLE

Exploring Mixed Hydrotropy Concept in HPTLC Densitometric Estimation of Telmisartan

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Received: 02nd March, 2024; Revised: 15th July, 2024; Accepted: 09th August, 2024; Available Online: 31st August, 2024

ABSTRACT

Analysis of the poorly water-soluble drugs most frequently carried out by using organic solvents like methanol, ethanol, chloroform, acetonitrile, and hexane. Most of them have toxic effects on humans as well as the natural ecosystem. The volatile nature of organic solvents is a major source of inaccuracy. So, the current study provides the best approach to replace organic solvents as hydrotropic solubilization techniques and developed a green, eco-friendly method to estimate telmisartan by high-performance thin-layer chromatography (HPTLC). Using silica gel coated (60 F254) TLC plates, chromatographic separation was achieved with a mobile phase 30% Sodium Benzoate (SB): 20% sodium acetate (SA): 0.5% citric acid (CA) (6:3:0.5 v/v/v). The retention factor for telmisartan was 0.55. Concentrations were linear in between 500 to 900 µg/mL with a regression coefficient was 0.9930. This approach was successfully validated as per the International Conference on Harmonization and it exhibits satisfactory results for all parameters. The developed approach is capable of being used to conduct routine evaluations of telmisartan in bulk and marketed formulation.

Keywords: Telmisartan, HPTLC, Mixed hydrotropy.

International Journal of Pharmaceutical Quality Assurance (2024); DOI: 10.25258/ijpqa.15.3.16

How to cite this article: Sheetal C, Chopade V. V, Vasudha B. Exploring Mixed Hydrotropy Concept in HPTLC Densitometric Estimation of Telmisartan. International Journal of Pharmaceutical Quality Assurance. 2024;15(3):1197-1200.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Awareness of the effects of hazardous substances on the environment and health has increased recently. The use of green chemistry concepts in research, development, and implementation has, therefore received a lot of attention in efforts to reduce them.

Telmisartan (TEL) chemically is 2[p-[[4-methyl-6(N-methylbenzo-imidazolyl)-2-propylbenzoimidazolyl] methylphenyl]Benzoic acid (Figure 1). It acts by inhibiting the effects of an angiotensin receptor and is used in the treatment of high blood pressure. It also works well for treating high blood pressure whether used either by alone or in conjunction with other medications.[1-5]

Enhancement of water solubility of lipophilic drugs is a major task for analytical chemists and hence safe, acceptable, green chemistry approach is utilized precluding organic solvents. Mixed hydrotropy is one of the concepts that increases the water solubility of lipophilic substances.

According to the literature survey, various UV-visible spectroscopic[6-9] HPTLC[10,11] methods are available for the determination of TEL alone and in combination. Very few methods UV-visible spectroscopic[12,13] methods are available using the hydrotropy approach. There isn't a published high-performance thin layer chromatography (HPTLC) method for estimating TEL utilizing the hydrotropic concept. For the purpose of estimating TEL in bulk and marketed formulation, an eco-friendly, economical, straightforward, and accurate HPTLC approach has been devised in the current work.

MATERIAL AND METHOD

Materials

TEL was obtained from Lupin Pharmaceuticals Pvt, Co. Pune, Maharashtra, as a gift sample. Sodium benzoate, sodium acetate, citric acid and piperazine are of AR grade and procured from Sisco Research Laboratories Pvt. Ltd, Mumbai, Maharashtra.

Instrumentation and Chromatographic Conditions

On 20X10 cm aluminium TLC plates 60 F_{254} pre-coated with 250 m layers of silica gel, chromatography was carried out. Samples were applied using a sample applicator [Camag Linomat-V (Switzerland)] provided with a Hamilton micro-syringe (100 L). The adjacent band's 20 mm separation was optimized, and the application rate was kept constant at 0.1 L/second. After that, the plates were treated for 10 minutes in a pre-saturated twin-wall glass container (20 X 10 cm^2). The time for saturation was 30 minutes.

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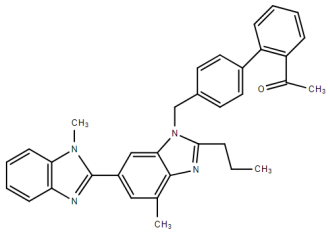

Figure 1: Structure of TEL

At room temperature, ascending development was carried out to approximately 80 mm from the point of application with a mobile phase consisting of 30% sodium benzoate (SB): 20% sodium acetate (SA): 0.5% citric acid (CA) (6:3:0.5 v/v/v) previously saturated to 30 min. After drying in the current air without the use of an air dryer, the plates were scanned at 296 nm using a Camag TLC scanner that was controlled by Win Cats software. Dimensions of the slit (4 X 0.2 mm) were optimized and kept constant during the experiment.

Preliminary Solubility Studies of TEL

The solubility of TEL was determined at 27°C. In two screws capped 25 mL of volumetric flask, a definite amount of drug was added with aqueous systems, viz combination of distilled water and hydrotropic agent in various concentration ranges. Various hydrotropic agents were used, such as sodium benzoate, Sodium acetate, urea, citric acid, and piperazine. Compared to the solubility study in other solvents, it has been found that the solubility of TEL was multiplied in 10% piperazine.

Preparation of Standard Solution

Precisely measured 0.1 g of TEL was placed into a volumetric flask (100 mL). Add 60 mL of 10% piperazine, shake well and volume make up to mark using distilled water (1000 µg/mL). TEL solution was scanned in timed scanning mode for 30 minutes. According to the chemical spectrum, the drug is stable in a hydrotropic solution.

Selection of Wavelength

A suitable aliquot was taken and diluted to 10 mL to prepare a concentration 10 µg/mL. This solution is subjected to UV scan between 200 to 400 nm.

Mobile Phase Selection and Optimization

A number of trial-and-error techniques were used to find the appropriate solvent systems. For the HPTLC analysis of TEL, a solvent system of 30% SB, 20% SC, and 5% CA in a ratio of 6:5:0.5 was chosen through trial and error. The drug was isolated with good resolution (0.555) in the developed mobile phase.

Analysis of Sample

About 20 tablets (Telista 40 mg) were weighted, triturated and fine powder that equated to 0.1 g of TEL was accurately measured and put into a volumetric flask of capacity 100 mL. About 60 mL 10% piperazine was added to the flask. Sonicate the solution for 15 minutes and make up the volume by using distilled water (1000 µg/mL). Filter out the solution with Whatman filter paper. A suitable aliquot was taken to prepare solutions of concentration 800 µg/mL with distilled water. This solution was put to a thin layer chromatography (TLC) plate, then developed and scanned. Triplicate analyses were performed.

Method Validation

The ICH guideline Q2 (R1) was utilized to validate the created HPTLC method for various validation parameters.[14-16]

Linearity

A linearity study was carried out and was found to be linear over concentrations 500, 600, 700, 800 and 900 µg/mL with regression coefficient showed from the calibration plot was (r^2) 0.9930.

Accuracy (recovery)

Three different degrees of accuracy were studied: 80, 100, and 120%. The study was conducted using the standard addition method, in which three distinct known concentrations of standard API were added to a commercial formulation.

Precision

The developed method for precision study was validated based on differences within a day, in between days and consistency. The result was expressed in %RSD.

Robustness

Robustness was evaluated by making small, purposeful adjustments to the established HPTLC method's parameters (mobile phase volume and saturation duration).

LOD and LOQ

The values of LoD and LoQ were calculated from the slope and standard deviation of the calibration graph.

RESULT AND DISCUSSION

Linearity

The developed method was linear over concentrations of 500, 600, 700, 800, and 900 µg/mL (Figures 2 and 3).

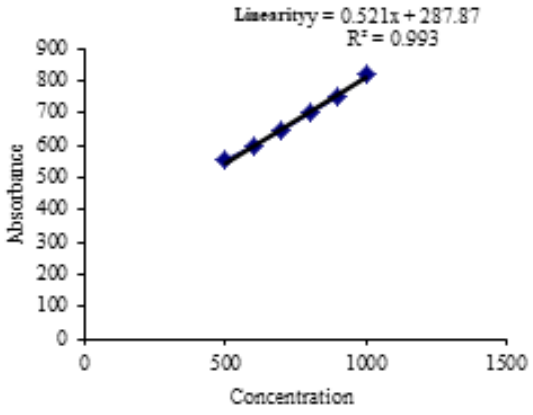

Figure 2: Linearity of TEL

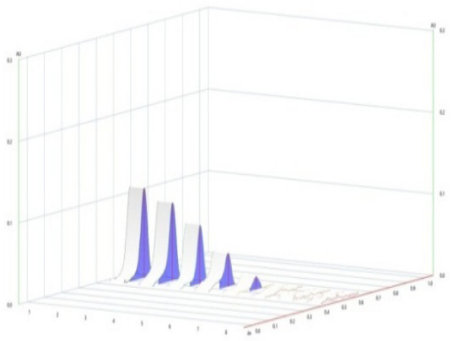

Figure 3: Graph of linearity of TEL

Analysis of Marketed Formulation

Table 1 shows the analysis of marketed formulations and Figure 4 shows the peak of a sample (Telista 40 mg)

Accuracy

The accuracy study was conducted by evaluating the recovery of TEL. The %recovery was found to be 100 ± 0.94, 100 ± 0.35, and 100 ± 0.29 for 80, 100 and 120% of target concentrations for TEL (Table 1). The values near 100% indicated the method's accuracy.

Precision

Three different concentrations were used for precision studies (within a day, in between days and consistency), which encompassed the whole range of the technique. The percentage RSD value was determined to be less than 2. A repeatability analysis was conducted by analyzing the target concentration six times over a short period of time, resulting in a %RSD value within limits, indicating that the approach is precise.

LOD and LOQ

The approach was confirmed to be specific, with no interference from excipients observed. Based on the experimental circumstances employed, the lowest limit of detection (LoD) was 24.577, while the lowest limit of quantification (LoQ) for TEL was 74.476. This means that the TEL can be correctly and precisely calculated, indicating the method's sensitivity. The summary of validation is presented in Table 2.

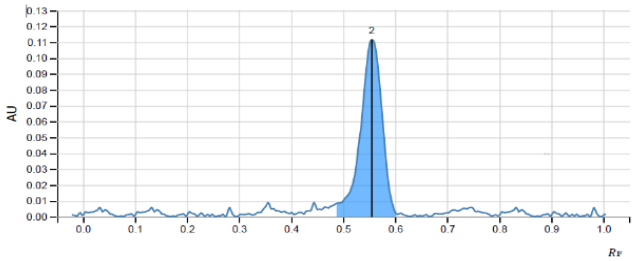

Figure 4: Peak of sample (Telista 40 mg)

Table 1: Analysis of marketed formulations

Sample	*Labeled claim*	*%Labeled claim ± SD*	*%RSD*
TEL	Telista 40 mg	100.03 ± 0.06	0.77

Table 2: Summary of validation

S. No	*Parameters*		*Results*
1.	Linearity and range (µg/mL)		500–1000 µg/mL
	Correlation coefficient		0.993
2.	Precision (%RSD)		
	Intra-day (n = 3)		0.35–0.50
	Inter-day (n = 3)		1.22–1.77
	Repeatability (n = 6)		1.17
3.	LoD (µg/mL)		24.577
4.	LoQ (µg/mL)		74.476
5.	Accuracy (Mean ± SD) (n = 3)	80%	100.00 ± 0.94
		100%	100.19 ± 0.35
		120%	100.07 ± 0.29

Table 3: Summary of robustness

Parameters	*Changes*	*Mean ± SD*	*%RSD*
Change in mobile phase	Mob. Phase I [30%SB:20% SC:5%CA (5:4:1)]	649.17 ± 5.19	0.80
	Mob. Phase II 30%SB:20% SC:5%CA (6:5:0.5)	663.50 ± 4.85	0.73
Change duration of saturation	25 minutes	704.67 ± 5.50	0.78
	30 minutes	698.83 ± 4.96	0.71
	35 minutes	704.00 ± 3.90	0.55
Change in analyst	Analyst I	11135.00 ± 3.0	0.03
	Analyst II	11095.00 ± 5.2	0.05

Robustness

There were several parameters for doing a robustness study, including changes in mobile phase composition volume. The chamber saturation time can also be altered for a robustness study (Table 3).

CONCLUSION

The hydrotropic approach was effectively used in the development of the HPTLC technique for the identification and quantification of TEL. The key characteristics of this approach are low cost and eco-friendly. The solubility of TEL was identified by using various hydrotropic agents. Statistical analysis shows that the approach is sensitive, precise, accurate and reproducible. The method was easily implemented for the regular analysis of TEL in bulk and in pharmaceutical formulation after it was satisfactorily validated in compliance with ICH guidelines.

ACKNOWLEDGMENT

The authors would like to thank Lupin Pharmaceuticals, Pune, India, for providing gift samples of TEL, Modern College of Pharmacy, Nigdi, Pune, for providing facilities for carrying out the work and Anchrom Enterprises PVT Ltd, Mulund, Mumbai, Maharashtra.

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