

Stability-Indicating RP-HPLC Method for Estimation of Miglitol in Bulk and Tablets

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Shrivastava, *et al.*: Stability-Indicating RP-HPLC Method for Miglitol

A selective and sensitive, stability-indicating reverse phase high performance liquid chromatography method has been first developed and validated for the estimation of miglitol in bulk and tablet dosages form. Samples were separated on a prepacked, Inertsil amino C₁₈ column (150×4.6 mm i.d.) using a mobile phase comprised of acetonitrile and monobasic sodium phosphate pH 7.5 (80:20, v/v) delivered at 1.5 ml/min flow rate. Detection was performed on a SPD-20A prominence UV/Vis detector at 220 nm. The retention time for miglitol was 13.93±0.0367. The method was validated in terms of linearity, precision, accuracy, ruggedness, and specificity, limit of detection and limit of quantification. The linearity (r²) and percentage recoveries of miglitol were 0.9986 and 99.85%. This method is suitable for routine estimation of miglitol in bulk and tablet dosages form.

Key words: Miglitol, RP-HPLC, stability indicating and method validation

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Miglitol, (2R,3R,4R,-5S)-1-(2-hydroxyethyl)-2-(hydroxymethyl)-3,4,5-piperidine-triol), a desoxyojirimycin analog, which is an oral alpha-glucosidase inhibitor that delays digestion of ingested carbohydrates resulting in a smaller rise in blood glucose concentration following meals^[1]. A few analytical methods have been reported for the determination of the studied drug. The reported methods for estimation of miglitol were spectrophotometric methods^[2], HPLC-MS^[3-5] and capillary electrophoresis^[6]. Even though various methods were reported in the literature for estimation of miglitol individually or in combination with other drugs no method had been reported for estimation of this drug using HPLC in bulk drug and tablet dosage form. The present study was aimed to development and validation of stability-indicating analytical method for miglitol in bulk and pharmaceutical dosage form, according to the ICH guidelines^[7].

The analysis was performed on a high performance liquid chromatographic (HPLC) system equipped with a prominence LC pump, a manual-sampler

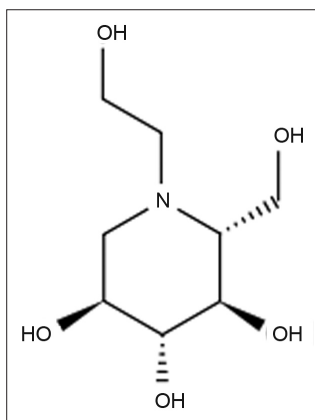


Fig. 1: Chemical structure of miglitol

and a SPD-20A prominence UV/Vis detector at 220 nm. The analytical column was a prepacked, inertsil amino C₁₈ column (150×4.6 mm i.d.) and column temperature was set to 55°. The mobile phase consisted of acetonitrile and monobasic sodium phosphate buffer, pH 7.5 (80:20, v/v) at an isocratic flow rate of 1.5 ml/min. The sample injection volume was 20 µl and run time was 30 min. Data acquisition and processing was performed with the Spinchrom chromatographic software.

Miglitol tablets were obtained from Glenmark Pharmaceutical Pvt. Ltd., (Mumbai, India). Miglitol reference a standard (99.87% purity) was supplied by Glenmark Pharmaceutical Pvt. Ltd., (Mumbai, India). The chemical structure of miglitol is shown in fig. 1. HPLC grade acetonitrile and water were purchased from Merck Chemicals Mumbai, India. Other chemicals were all of analytical grade and were used as received.

Standard stock solution (1 mg/ml) of miglitol was prepared in diluent (redistilled water and acetonitrile in proportion of 80:20 (v/v) by transferring accurately 100 mg of miglitol working standard into a 100 ml volumetric flask, and dissolves with 50 ml diluent and sonicate for 10 min. Dilute up to the mark with diluent. Filter the solution through a 0.45 µ membrane filter. The working standard solution for the calibration curve was prepared in the concentration range of 2-100 µg/ml of miglitol.

Twenty tablets, (Mignar, Glenmark), each containing 50 mg of miglitol were weighed and finely powdered. A quantity of powder equivalent to 50 mg of miglitol was weighed and transferred to a standard flask (50 ml). About 30 ml of diluent was added and shaken. The mixture was then sonicated in ultrasonic bath

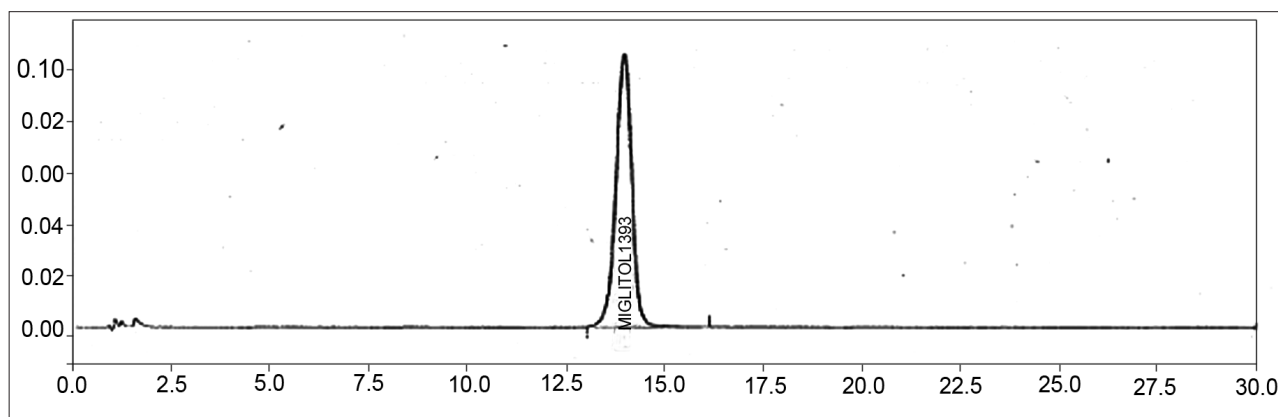


Fig. 2: Typical chromatogram of miglitol

for 10 min and the volume was made up to 50 ml using the diluent. The solution was filtered with a Whatman filter paper No.1. Before injection, standard and sample solutions were filtered through 0.45 µm syringe filter. Then 20 µl of standard and sample solutions were injected into the column and chromatogram was recorded. A typical chromatogram of miglitol was shown in (fig. 2).

The peak area, retention time (Rt), capacity factor, theoretical plate, and peak symmetry were calculated five times for the standard solution. The values

TABLE 1: SYSTEM SUITABILITY

Parameter	Miglitol (n=5)
Capacity factor	$\bar{X} = 0.99506 \pm 0.0107$ SD = 0.0122 RSD = 1.23%
Theoretical Plate (Per column length)	$\bar{X} = 5858.71 \pm 25.3004$ SD = 28.8631 RSD = 0.49%
Asymmetry of the peak	$\bar{X} = 1.01 \pm 0.0144$ SD = 0.0164 RSD = 1.65%
Retention time (min)	$\bar{X} = 13.93 \pm 0.0367$ SD = 0.0418 RSD = 0.30%
Peak area	$\bar{X} = 2982175 \pm 11280.7379$ SD = 12869.25 RSD = 0.43%

\bar{X} is mean ± percentage range of error (within 95% confidence limits), SD is standard deviation, RSD is relative standard deviation and 'n' is average of 5 samples.

TABLE 2: SUMMARY OF ANALYTICAL METHOD VALIDATION

Validation parameters	Miglitol
Specificity	Specific
Accuracy (Recovery)	99.85%
Intraday precision (RSD)	0.1978%
Interday precision (RSD)	0.1783%
Linearity (r^2)	0.9986
Robustness (RSD)	0.51%
LOD (ng/ml)	5.8
LOQ (ng/ml)	18.7

RSD is relative standard deviation, r^2 is correlation coefficient, LOD is the limit of detection and LOQ is limit of quantification.

TABLE 3: RECOVERY STUDIES

Analyte	Labeled amount (mg)	Amount added (mg)	% Label claim (mg) n=3*	%Recovery	Average % recovery
Miglitol	50	45	$\bar{X} = 95.3409 \pm 1.0969$ SD = 0.9693 RSD = 1.01669%	100.36	99.85
		50	$\bar{X} = 99.4135 \pm 1.4519$ SD = 1.283033 RSD = 1.290602%	99.41	
		55	$\bar{X} = 04.7758 \pm 1.3548$ SD = 1.1972 RSD = 1.14260%	99.79	

\bar{X} is mean ± percentage range of error (within 95% confidence limits), SD is standard deviation, RSD is relative standard deviation and 'n' is average of 3 samples.

obtained demonstrated the suitability of the system for the analysis of the miglitol. System suitability parameters fall within 2% coefficient of variation (%RSD) during routine performance of the method. The summary of the system suitability results were showed in the (Table 1).

Response of miglitol was determined for the detector to be linear, over the range of 2-100 µg/ml (2, 5, 10, 25, 50, 100). Each concentration was injected duplicate to get reproducible response. The proposed method was evaluated by its correlation coefficient value calculated in the statistical study. They were represented by the correlation co-efficient (Table 2).

The accuracy of the method was determined by recovery experiments. The recovery studies were carried out 9 times and the percentage recovery, standard deviation and coefficient of variation was calculated. From the data obtained, recoveries of standard drug were found to be accurate (Table 3). The coefficient of variation of interday and intraday precision obtained was less than 2%. The intraday and interday precisions of miglitol were 0.1978 and 0.1783, respectively. From the data obtained, the developed HPLC method was found to be precise and accurate.

In the chromatograms of the formulations, some additional peaks were observed which may be due to excipients present in the formulations. These peaks however didn't interfere with the standard peak, which demonstrate that the assay method is specific. Furthermore, the purity of the peak was studied by peak purity studies. The results revealed that the peak is free from interferences, which shows that the HPLC method is specific.

The limit of detection (LOD) and quantification (LOQ) of the developed method were determined

by injecting progressively low concentrations of the standard solutions using the developed method. The LOD and LOQ of miglitol were found to be 5.8 and 18.7 ng/ml, respectively. The robustness of the method was studied by deliberate changes in the method like percentage organic content, alteration in pH of the mobile phase, changes in the wavelength. It was observed that there was no marked changes in the chromatograms demonstrate that the HPLC methods have developed are robust.

Stress degradation study using acid and alkali hydrolysis, chemical oxidation and dry heat degradation was carried out and interference of the degradation products were investigated. Miglitol was weighed (50 mg) and transferred to a 50 ml volumetric flask and diluted up to the mark with diluent. This stock solution was used for forced degradation studies. Forced degradation in basic media was performed by taking 1 ml stock solution of miglitol (1000 µg/ml) in a 50 ml volumetric flask and 5 ml of 1N NaOH was added. The flask was heated in a water bath at 60° for 1 h. After heating solution was neutralized and diluted up to the mark with diluents. Appropriate aliquot was taken from the above solution and diluted with diluent to obtain final concentration of 10 µg/ml of miglitol. Similarly, forced degradation in acidic medium was performed using 1N HCl. To perform oxidative stress degradation, appropriate aliquots of stock solutions of miglitol (1 mg/ml) was taken in 50 ml volumetric flask and 5 ml of 3% hydrogen peroxide was added. The mixture was heated in water bath at 60° for 1 h. Further the solutions were diluted with diluent to obtain final concentration of 5 µg/ml of miglitol. To study dry heat degradation, solid drug were exposed in oven at 100° for 24 h. After 24 h of heating, 50 mg miglitol was weighed and transferred to two separate volumetric flasks (50 ml) and diluted up to the mark with the mobile phase. Solution was further diluted by taking appropriate aliquot in 10 ml volumetric flask to obtain final concentration of 10 µg/ml of miglitol. All the reaction solutions were injected in the liquid chromatographic system and chromatograms were recorded. The summary of the system suitability results were showed in the (Table 4).

This method is simple, specific, and easy to perform and requires short time to analyze the samples.

TABLE 4: SUMMARY OF FORCED DEGRADATION STUDY

Sample (condition)	Percentage degradation
Acid degradation	12.2
Alkali hydrolysis	0.0
Chemical oxidation	10.4
Dry heat degradation	0.0

Low limit of quantification and detection makes this method suitable for use in quality control. This method enable for determination of miglitol because of good symmetric chromatographic peak. The method was found to be linear, precise, accurate, rugged and robust. The proposed HPLC method required fewer reagents and materials, and it is simple and less time consuming. This method could be used in quality control test in pharmaceutical industries.

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