Research Article

Quantitative Estimation of Sorafenib Tosylate Its Pure Form and in Its Tablet Formulation by RP-HPLC Method

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A simple, accurate, specific reverse-phase, high-performance liquid chromatography method has been developed for the determination of sorafenib tosylate in its pure form and its tablets. In this method, sorafenib tosylate was eluted by isocratic mode using a Phenomenex Luna C18 column by a mobile phase composition of acetonitrile and water in the ratio of 82.5 : 17.5, v/v. The flow rate was 1.5 mL/min. The eluted drug was monitored at 265 nm and the method was found to be linear from 5 to 80 µg/mL. The method was validated by linearity, precision, accuracy, LOD, and LOQ. The accuracy report denotes that there is not any interference of additives used in the formulation.

1. Introduction

Sorafenib tosylate is chemically 4-(4-{3-[4-chloro-3-(trifluoromethyl)phenyl]ureido}phenoxy)-N-2-methylpyridine-2-carboxamide 4-methylbenzenesulfonate. The drug was approved for the treatment of primary kidney cancer and advanced primary liver cancer. Sorafenib tosylate was estimated by RP-HPLC in human serum [1, 2]. It was estimated in bulk and in tablets by RP-HPLC [3], HPTLC [4], colorimetric estimation [5], and by UV method [6, 7]. The present work aims to develop a simple, precise, and accurate RP-HPLC method for the estimation of sorafenib tosylate in pure drug and in its tablet formulation.

2. Experimental Methods

Sorafenib tosylate pure drug was obtained as a gift sample from Natco pharma (Hyderabad, India). All the reagents used were HPLC grade.

2.1. Instrumentation. The HPLC experiment was carried out in a Shimadzu HPLC system equipped with Phenomenex

Luna C18, 5 µm (4.6 × 250 mm) column, two LC-20AD pumps, SCL-10AVP system controller, Rheodyne injector with 50 µL loop, and SPD-20A UV-visible detector, and LC Solution software was used. All the reagents used were HPLC grade. The mobile phase was a mixture of acetonitrile and water (82.5 : 17.5, v/v) that was set at a flow rate of 1.5 mL/min.

2.2. Drug Stock Solution. Stock solution of sorafenib tosylate was prepared by dissolving accurately weighed 100 mg of the pure drug in 100 mL of mobile phase (final concentration, 1 mg/mL). The prepared stock solution was stored at 4°C and protected from light.

2.3. Calibration Curve. From the above stock solution, 10 mL was taken and diluted to 100 mL with mobile phase. Subsequent dilutions of this solution ranging from 5–80 µg/mL were made in 10 mL volumetric flasks. The solutions were filtered through 0.45 µm membrane filters and then 50 µL of filtrate was injected each time into the column at flow rate of 1.5 mL/min. Evaluation of the drug was performed with

TABLE 1: Assay results and precision studies.

Sample	Labeled amount (mg/tablet)	Amount found (mg/tablet)	(%) label claim ^a $\pm$ S.D	Precision ^b	
				Inter-day	Intra-day
Sorafenib tablets	200	199.76	99.98 $\pm$ 0.297	0.5998	0.2975

^a Average of six determinations.^b %RSD of six determinations.

TABLE 2: Recovery study.

Sample	Label claim (mg/tablet)	Amount of drug added (μ g/mL)	Amount of drug recovered (μ g/mL)	Percentage recovery $\pm$ SD ^a
Sorafenib tablets	200	32	32.08	100.23 $\pm$ 0.070
		40	39.92	99.81 $\pm$ 0.236
		48	47.98	99.95 $\pm$ 0.058

^a Mean of six determinations.

UV detector at 265 nm. Peak area was recorded for all peaks. A plot of peak area versus the respective concentration gives the calibration curve. The regression of drug concentration over the peak area was computed. Unknown samples were estimated by reference to this calibration curve.

2.4. Sample Preparation. Twenty tablets were weighed accurately and crushed to fine powder. From that, the amount of powder equivalent to 100 mg of sorafenib tosylate was weighed accurately and transferred to a 100 mL volumetric flask. Mobile phase (50 mL) was added and the mixture was sonicated for 10 min, for complete extraction of the drug, and the solution was diluted to volume with mobile phase. Then solution was centrifuged at 4000 rpm for 10 min, and the clear supernatant was collected and filtered through a 0.2 μ m membrane filter. From this solution 10 mL was taken and diluted to 100 mL with mobile phase, again 4 mL was diluted to 10 mL to get 40 μ g/mL solution, of which 50 μ L was injected for HPLC analysis.

3. Results and Discussion

A typical chromatogram of sorafenib tosylate was shown in Figure 1. The retention time for sorafenib tosylate was 3.4 min. Flow rate was fixed at 1.5 mL/min, which gives tailing factor in the acceptable limit. The peak areas from such different concentrations of 5 to 80 μ g/mL were calculated. A good linear relationship ($r^2 = 0.998$) was observed between the concentration drug and the respective peak area. The regression curve was constructed by linear regression fitting. The intraday and interday variations of the method were determined, a low coefficient of variation was observed. This shows that the present HPLC method is highly precise. To ensure accuracy of the method, recovery studies were carried out mixing a known quantity of drug with preanalyzed sample and the contents were reanalyzed by the proposed method. The recovery was about 99.95% to 100.23% (Table 2), indicating the high accuracy of the proposed HPLC method. The drug content in tablets was quantified using the proposed analytical method and the results are shown in Table 1.

FIGURE 1: A typical chromatogram of sorafenib.

Chromatographic parameters such as peak asymmetry and capacity factor were found to be 1.03 and 0.921, respectively. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.133 and 0.403 μ g/mL, respectively. The precision of the method was calculated in terms of the relative standard deviation. Low values of relative standard deviation indicated high precision and accuracy of the proposed method.

4. Conclusion

The developed RP-HPLC method was simple, sensitive, precise, and accurate and hence can be used in routine for the determination of sorafenib tosylate in pure as well as in tablets.

Conflict of Interests

The authors declare that there is no conflict of interests.

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