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Short communication

Assay of sertraline in tablets and drug substance by liquid chromatography

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Abstract

A high-performance liquid chromatography isocratic procedure was developed for the assay of sertraline in drug substance and tablets. The chromatographic system consists of a RP-8 column (125 × 4 mm, 5 μm), a mobile phase composed of acetonitrile and sodium phosphate buffer, pH 5.5 (7:3), flow rate of 1.0 ml.min^{-1} and UV detection at 270 nm. The method validation yielded good results. The coefficient of variation varied between 0.19 and 1.04% and accuracy of 99.18% was found. Calibration curve was linear between 0.5 and 2.5 mg.ml^{-1}; its correlation coefficient was 0.9999.

Keywords: Sertraline; High-performance liquid chromatography assay; Quality control

1. Introduction

Sertraline is a potent selective serotonin reuptake inhibitor (SSRI) that has established efficacy in the treatment of depression, obsessive-compulsive disorder, depression relapse and social phobia [1,2]. It is unrelated to tricyclic, tetracyclic or other available antidepressant agents (Fig. 1) [3].

Sertraline seems to be better tolerated than imipramine in long-term treatments of chronic depression [4]. It has some characteristics that offer advantages over the other members of this class of antidepressants in the treatment of elderly patients with major depression. The pharmacokinetic of sertraline is the same in both elderly and younger patients, whereas elderly, with other drugs of this class, develop higher plasma levels. It also presents less risk of drug interactions mediated by the cytochrome P-450 enzymatic complex [5].

For its analytical determination in formulated products and in drug substance, the literature indicates ultraviolet and visible spectrophotometry, potentiometric titration and chromatography [3,6,7]. It is not included in any pharmacopoeia.

The aim of this study was to develop an easy, fast and accurate high-performance liquid chromatography (HPLC) method to analyse the quantity of sertraline in drug substance, tablets or capsules.

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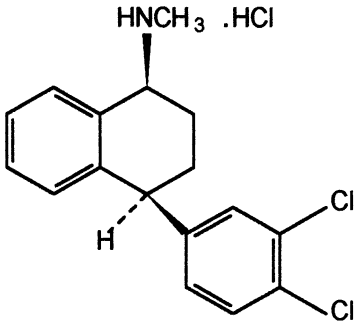

Fig. 1. The chemical structure of sertraline hydrochloride.

2. Experimental

2.1. Reagents and solutions

Acetonitrile of HPLC grade was used for the preparation of solvent mixture and of the mobile phase. The water used was purified by a Millipore® system. Dibasic and monobasic sodium phosphate were of analytical grade. The solvent mixture, used for diluting all the solutions of sertraline, was composed by a mixture of acetonitrile–water (8:2, v/v). A solution of acetonitrile–sodium phosphate buffer, pH 5.5 (7:3, v/v) was used as the mobile phase. To prepare the buffer solution, 6.5 g of sodium phosphate monobasic and 0.15 g of anhydrous dibasic sodium phosphate were weighed and dissolved in 1000 ml of purified water. The pH was adjusted to 5.5 ± 0.1, with sodium hydroxide 1 N or orthophosphoric acid 18% (v/v).

2.2. Samples

The reference substance, sertraline hydrochloride (assigned purity 100.46%) and tablets were donated by a pharmaceutical industry. The samples were: two drug substance, two capsules manufactured in local compounding pharmacies (sertraline 50 mg, excipients q.s.p. 301.65 and 210.78 mg) and a sample of tablets available commercially (sertraline 50 mg, excipients q.s.p. 205.14 mg).

2.3. Instrumentation and conditions

Liquid chromatograph (Shimadzu, LC-10 AD) with a manual sample injection Reodyne® valve with a 20 μl loop; a variable UV detector (Shimadzu SPD-10AV) set at 270 nm; a Merck LiChrospher® 100 RP-8 (125 mm × 4 mm i.d., 5 μm particle size) column. An electronic integrator (Shimadzu C-R6A) was used to calculate peak areas. The flow rate of the mobile phase was adjusted to 1.0 ml min^{-1}. All the samples were filtered before injection.

2.4. Procedure

2.4.1. Sertraline hydrochloride reference substance

Solutions of the reference substance were prepared by transferring a quantity of the substance, accurately weighed, to a volumetric flask and diluting with the solvent mixture to obtain solutions containing 1.5 mg ml^{-1} (assay for drug substance) and 0.75 mg ml^{-1} (assay for tablets and capsules).

2.4.2. Assay of sertraline in drug substance

Solutions were prepared by transferring about 37.5 mg, accurately weighed, to a 25 ml volumetric flask, in order to obtain a solution containing 1.5 mg ml^{-1}.

2.4.3. Assay of sertraline in tablets and capsules

Twenty tablets/capsules were weighed to get the average weight. Samples of the powdered tablets were transferred to 25 ml flasks; 15 ml of the solvent mixture were added, shaken for 10 min by a mechanical shaker and diluted to volume with the diluent, to provide a solution containing 0.75 mg ml^{-1}.

2.4.4. Accuracy test

To confirm the accuracy of the proposed method, the recovery test was performed, following the recommendations of USP 24 [9]. It was determined by adding known amounts of the sertraline hydrochloride reference substance (0.6, 0.75 and 0.9 mg ml^{-1}) to the sample at the beginning of the process.

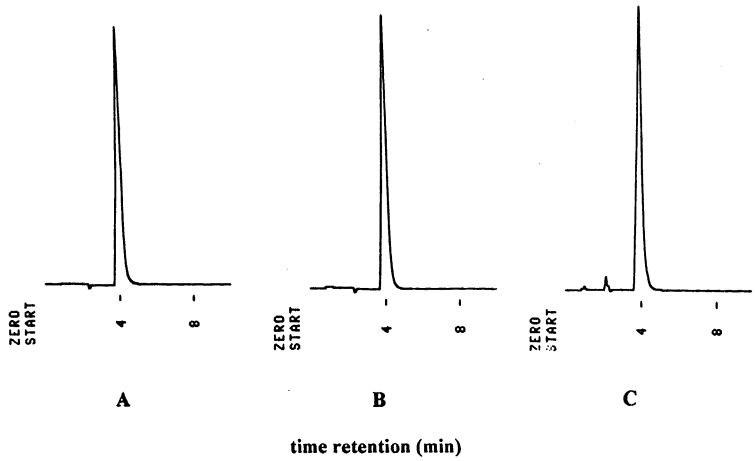

Fig. 2. HPLC chromatogram of (A) the sertraline reference substance, (B) sertraline tablets and (C) sertraline capsules.

2.4.5. Linearity and precision

The linearity of the calibration curve was determined for intra- and inter-day experiments on two different days. Calibration curve was constructed in a range of 0.5–2.5 mg ml^{-1}. Repeatability was evaluated and expressed as the relative standard deviation (RSD; coefficient of variation) [9].

3. Results and discussion

Like other members of the SSRI group, sertraline offers an alternative to treatment with a tricyclic agent in depression. Even so, it is not described in any pharmacopoeia. The goal of this study was to develop an HPLC assay for the determination of sertraline in drug substance and tablets.

The accuracy and precision of HPLC data begin with a well-behaved chromatographic system. The system suitability specifications and tests are parameters that provide assistance in achieving this purpose. Some of them are the theoretical plate number, the injection precision, the capacity factor (K') and the resolution. The theoretical plate number (N), that is a measure of column efficiency, was determined ($N = 2600$). Injection precision expressed as RSD was determined: the values varied between 0.1 and 0.75%. The general recommendation is RSD $\leqslant$ 1.0% [8]. The retention time (t_R) of sertraline was 3.8 min that provides adequate run time analysis (Fig. 2). The capacity factor, based on the t_R value, was calculated ($K' = 2.88$). According to CDER [8], the recommended value is $K' > 2$. The solutions used on the assay were kept at room temperature and evaluated in a 24-h period. No differences on peak area were found, indicating the stability of the analyte in solution on this specified time (results not showed).

The calibration curves for sertraline hydrochloride were constructed by plotting the peak areas versus concentration. It was found to be linear with a correlation coefficient of 0.9999; the linear regression equation $y = 124\,136 + 3\,491\,562x$. The relative deviation of the intercept of the two curves was 4.58% and the relative deviation of the slope was 1.19%.

The results of sertraline determination in all the samples used are shown in Table 1. The precision of the method can be evaluated by the low CV values observed in the same table.

To evaluate the accuracy of the proposed method applied to the drug substance, we compared these results with those obtained from the UV method described in the literature [3]. The average value found by the UV method ($n = 5$) was 98.74% (CV 0.42%) for D1, and 100.45% (CV 1.53%) for D2. From the statistical analysis of the UV and HPLC methods it could be concluded

Table 1
Analysis results for sertraline as drug substance (D1, D2), tablets (T) and capsules (C1, C2) by HPLC method

Sample	Theoretical amount (mg)	Experimental amount (mg)	Purity[a]	CV (%)
D1	–	–	98.92	1.04
D2	–	–	99.64	0.88
T	50	49.51	99.01	0.19
C1	50	50.07	100.14	0.81
C2	50	49.68	99.37	0.88

[a] Mean of nine determinations for D1, D2 and five determinations for T, C1 and C2.

Table 2
Recovery of a standard solution added to tablet (T) and capsules (C1, C2) samples by HPLC

Sample	Added (mg ml^{-1})	Found[a]	Recovery (%)
T	0.60	0.5931	98.85
	0.75	0.7355	98.07
	0.90	0.8902	98.91
C1	0.60	0.5939	98.98
	0.75	0.7661	102.15
	0.90	0.9199	102.21
C2	0.60	0.5869	97.81
	0.75	0.7305	97.40
	0.90	0.8839	98.21

[a] Each value is the mean of two independent samples.

that no differences between them was found and that they were statistically equivalent, according to the Student-t test ($P < 0.05$).

The results of the accuracy tests can be observed in Table 2. The average recovery was 99.18%, confirming the accuracy of the proposed method.

4. Conclusions

The obtained results support the conclusion that the proposed method is accurate, precise, rapid and adequate to determine the content of sertraline in drug substance and formulated products.

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