Research Article

HPLC determination of Escitalopram in tablet dosage forms

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Abstract

Purpose: A simple, specific, precise, and accurate reversed phase liquid chromatographic (RP-LC) method has been developed for the determination of Escitalopram in tablet dosage form.

Methods: The chromatographic separation was achieved on a LiChrosorb C18, 250 mm x 4.6 mm, 5 μm column at a detector wavelength of 270 nm and a flow rate of 1.0 ml/min. The mobile phase was composed of methanol, acetonitrile (70:30 v/v). The retention time of Escitalopram was 5.49 min. The method was validated for the parameters like specificity, linearity, precision, accuracy, limit of quantitation and limit of detection.

Results: The method was found to be specific as no other peaks of impurities and excipients were observed. The square of correlation coefficient ($R2$) was 0.9999 while relative standard deviations were found to be <2.0%.

Conclusion: The proposed RP-LC method can be applied for the routine analysis of commercially available formulations of Escitalopram.

Introduction

Escitalopram (Cipralex, Lexapro, Seroplex, Sipralexa) is the (S)-enantiomer of the racemic selective serotonin reuptake inhibitor (SSRI) antidepressant citalopram (Fig. 1) (Peikova et al. 2014a, 2014b). Clinical studies have shown that Escitalopram is effective and well tolerated in the treatment of depression and anxiety disorders. Following oral administration, escitalopram is rapidly absorbed and reaches maximum plasma concentrations in approximately 3–4 hours after either single-or multiple-dose administration. (ClinCalc 2021; DailyMed 2021; Niranjan 2007; Palmer et al. 2002).
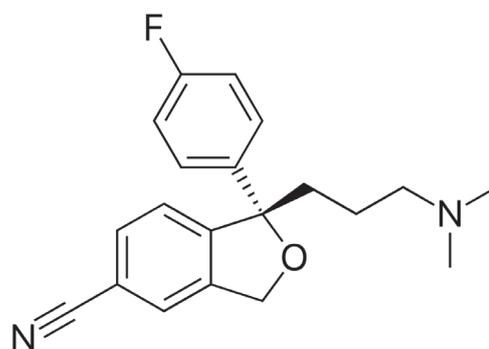

Figure 1. Structure of Escitalopram

PENSOFT

Escitalopram is unique among SSRIs in that it stabilizes its binding to the high-affinity binding site of the serotonin transporter protein via an allosteric effect at the low-affinity binding site. In vivo and in vitro studies have shown escitalopram to be approximately twice as potent as citalopram in inhibiting serotonin reuptake. It is highly selective for the serotonin transporter protein and shows no or very low affinity for other receptors or ion channels. In vivo, escitalopram was four times more potent than citalopram in reducing firing activity of presumed serotonergic neurons in rat brain (Dhillon et al. 2012). It is on the World Health Organization's List of Essential Medicines (WHO 2021).

Common side effects include nausea, trouble sleeping, sexual problems, shakiness, feeling tired, and sweating (Cascade et al. 2009). Serious side effects include an increased risk of suicide in those under the age of 25, serotonin syndrome, glaucoma, and QT prolongation. It should not be used in persons who take or have recently taken a MAO inhibitor (Carandang et al. 2011; Cohen 2007; Pedersen 2005). Antidepressant discontinuation syndrome may occur when stopped. There are concerns that use during pregnancy may harm the fetus (Hellerstein et al. 2004; Pittenger and Bloch 2014).

Escitalopram appears to have comparable efficacy and superior tolerability relative to other antidepressants. In the National Institute for Health and Clinical Excellence ranking of ten antidepressants for efficacy and cost-effectiveness, citalopram is fifth in effectiveness (after mirtazapine, Escitalopram, venlafaxine, and sertraline) and fourth in cost-effectiveness (Khoo et al. 2015; NICE 2010). The ranking results were based on a 2009 meta-analysis by Andrea Cipriani; an update of the analysis in 2018 produced broadly similar results. Evidence for effectiveness of Escitalopram for treating depression in children is uncertain (Cipriani et al. 2009).

European Pharmacopoeia recommended acid-base titration for analysis of Escitalopram in substance, UV-spectrophotometry for its determination in capsules as well as liquid chromatography for assay in gel. The aim of this paper is to develop a specific, precise and accurate chromatographic method that could be applied in quality control for the determination of Escitalopram in tablet in respect of European Pharmacopoeia and ICH requirements (Obreshkova and Peikova 2011; Peikova et al. 2013).

Materials and methods

Chemicals and Reagents Escitalopram was used as standard. Cipralex tablets containing 10mg active substance were obtained commercially. LC-grade methanol, acetonitrile Merck (Germany). All other chemical reagents were of analytical grade.

Instrumentation and chromatographic conditions

Chromatographic separation was performed on modular HPLC system LC-10A Shimadzu (Japan) arranged with a LC-10A pump, solvent degasser DGU-3A, Rheodyne injector, column oven CTO-10A, SPD-M10A diode array detector and communication bus module CBM10A. Separation was achieved isocratically with a LiChrosorb C18, 250 mm x 4.6 mm, 5 μm column eluted with a mixture of methanol, acetonitrile (70:30v/v) as the mobile phase at flow rate of 1 ml/min. Detection was carried out by absorbance at 270 nm. The analysis was carried out at an ambient temperature and injection volume was 20 μl. Preparation of standard solutions 10 mg of accurately weighed standard Escitalopram was dissolved and made up to mark with mobile phase in a 100 ml volumetric flask, to get primary stock solution of 200 μg/ml. Serial dilutions were made to obtain 5, 10, 25, 50, 75 and 100 μg/ml using mobile phase. All solutions were filtered through 0.45 μm membrane filter prior to use. Sample preparation A commercially available tablet formulation containing Escitalopram 10 mg was analyzed using this method. The content of 20 tablets was taken and powdered. The powder equivalent to 10 mg of Escitalopram was accurately weighed and transferred into a 100 ml volumetric flask. To this, 70 ml of mobile phase was added and sonicated for 10 min with occasional shaking to disperse and dissolve the contents. The volume was made up to 100 ml with the same diluent to give 500μg/ml. This solution was filtered through 0.45 μm membrane filter and diluted suitably using mobile phase to obtain 50 μg/ml solutions.

Results and discussion

The Fig. 2 showed typical chromatogram obtained from analysis of standard solution using the proposed method. The retention time observed –5.49 min permits a rapid determination of the drug, which is important for routine analysis.

System suitability parameters for this method were reported in Table 1.

Table 1. System suitability parameters for the method Parameter Escitalopram.

Retention time (min) ± % RSD	5.49±0.09
Tailing factor ± % RSD	0.82±0.15
Theoretical plates ± % RSD	7895±0.45
LOQ	0.5 μg/ml
LOD	0.1 μg/m

Validation study

The proposed method was validated as per ICH guidelines with respect to specificity, linearity, precision, and accuracy.

Specificity the specificity of the method was determined by checking the interference with the components from placebo. No interference was observed for any of the components like excipients of both drugs.
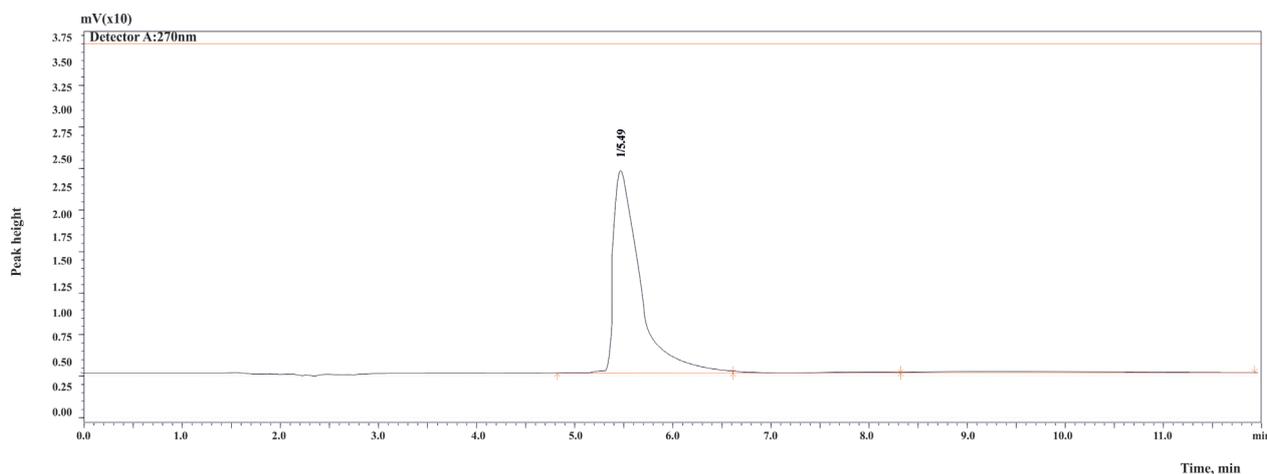
Figure 2. Chromatogram obtained from Escitalopram

Calibration and linearity

Calibration curve was constructed in the range of 5.00-100.0 µg/ml for ketoprofen to encompass the expected concentration in measured samples. The corresponding linear regression equation was y=14587.2x-1256.1 with square of correlation coefficient R2 of 0.9999. An excellent correlation existed between the peak areas and concentration of Escitalopram.

Precision

The precision of the method was evaluated by performing six independent determinations of the test sample preparation and calculating RSD (%). The RSD value measured during assessment of precision was <2.0% for Escitalopram, confirming the method is precise (Table 2).

Accuracy

To determine the accuracy of the method, the recovery was checked at three different concentration levels – 50,

100 and 150 %. Values of analytical recovery experiments were listed in Table 3.

Table 2. Precision of the method.

№	Amount found, mg/tablet	Statistical data
1.	50.03	
2.	49.98	Mean 49.66
3.	49.36	
4.	50.19	SD 0.434
5.	49.40	
6.	49.27	% RSD 0.87

Table 3. Results from study of accuracy.

Drug: Escitalopram			
Level (%)	50	100	150
Theoretical concentration (µg/ml)	25.90	50.25	75.25
Observed concentration (µg/ml)	24.98	50.1	75.20
	25.72	49.93	75.12
	25.81	50.20	75.18
Mean recovery (%) ± SD RSD (%)	99.11±1.31	99.81±0.642	63±0.620
	1.31	0.64	0.62

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