



Simultaneous UV Spectrophotometric Method for Estimation of Escitalopram Oxalate and Flupentixol Dihydrochloride in Tablet Dosage Form

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Abstract : A simple, accurate and precise spectrophotometric method has been developed for simultaneous estimation of escitalopram oxalate (ESC) and flupentixoldihydrochloride (FLU) in combined dosage form. Simultaneous equation method is employed for simultaneous determination of ESC and 230 from combined dosage forms. In this method, the absorbance was measured at 238 nm for ESC and 230 nm for FLU. Linearity was observed in range of 5-25 ug/ml and 0.5-2.5 ug/ml for ESC and FLU respectively. Recovery studies confirmed observed in range of 5-25 method and results were validated as per ICH guidelines. The method can be used for routine quality control of pharmaceutical formulation containing escitalopram oxalate and flupentixol.

Key words : Escitalopram oxalate, Flupentixoldihydrochloride, λ_{max} , Simultaneous equation method.

Introduction:

Escitalopram oxalate (ESC), chemically it is (S)-1-[3-(Dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydro-5-isobenzofuran-5-carbonitrile oxalate. It is an antidepressant, anti-obsessive-compulsive and anti-bulimic actions of ESC are presumed to be linked to its inhibition of CNS neuronal uptake serotonin at the serotonin reuptake pump of the neuronal membrane, enhancing the actions of serotonin on 5HT autoreceptors. SSRIs bind with significantly nor epinephrine receptors than tricyclic antidepressant drugs. It is official in Indian Pharmacopoeia^[1], United State Pharmacopoeia^[2].

Flupentixol hydrochloride (FLU), chemically it is (Z)-2-[4-[3-(2-(Trifluoromethyl) 9, thioxanthene-9-ylidene) propyl]piperazin-1-yl]ethyl dihydrochloride. FLU is a thioxanthene antipsychotic. The mechanism of action of FLU is not completely understood. FLU is a powerful antagonist of both D1 and D2 dopamine receptors, and an alpha-adrenergic receptor antagonist. Its antipsychotic activity is thought to be related to blocks postsynaptic dopamine receptors in the CNS. It is official in Indian pharmacopoeia, British pharmacopoeia³⁻⁴. The combination of Escitalopram oxalate and Flupentixoldihydrochloride is used in the treatment of depression.

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A combination of both drugs reduces the dose of individual drugs. Literature survey revealed that several methods are developed for ESC and FLU individually⁵⁻¹⁴. Liquid chromatographic methods and UV first derivative method have been developed for ESC and FLU in pharmaceutical dosage form¹⁵⁻¹⁷. To best of our knowledge none of the UV simultaneous equation method has been reported for estimation of ESC and FLU in combined dosage form. Hence, an attempt has been made to develop new UV simultaneous equation method for its estimation in pharmaceutical dosage formulations with good accuracy, simplicity and sensitivity.

Materials and Methods

Instrument:

A Shimadzu UV-1650PC UV/VIS Spectrophotometer was used with 1 cm matches quartz cell.

Materials:

Gift samples of ESC and FLU were procured from Shangrila Industries (P), Sikkim respectively. Tablets containing both drugs. Escitalopram oxalate (ESC) and Flupentixoldihydrochloride (FLU) were purchased from local pharmacy of commercial brand REXIPRA FX 5 (Intas pharmaceuticals)

Solvent used:

Mixture of Water:Methanol (50:50)

Preparation of stock Solution:

ESC (10mg) and FLU (10mg) were accurately weighed and transferred to two separate 10 ml volumetric flask, dissolved in Water:Methanol(50:50) solvent to obtain stock solution of 1000µg/ml. The stock solutions of both the drugs were further diluted separately with solvent to obtain 10µg/ml solution each and scanned in spectrum mode from 400-200nm. The overlain spectra of both the drug obtained (Fig No.1) to determine the λ_{max} . ESC has λ_{max} 238nm while FLU has λ_{max} 230nm.

Simultaneous Equation Method:

From the stock solution, working standard solution of drugs were prepared by appropriate dilution and were scanned in the entire UV range. Two wavelengths selected for the method are 238nm and 230nm that are absorption maximas of ESC and FLU respectively in Water:Methanol (50:50). A series dilution were prepared of standard solutions ESC and FLU 5-25µg/ml and 0.5-2.5 µg/ml respectively. The absorptivity coefficients of ESC within concentration range of 5-25 µg/ml and FLU within concentration range of 0.5-2.5µg/ml were determined at 238 nm and 230nm by calibration curve.

For the estimation of drugs in the commercial formulations, ten tablets containing 5mg of ESC 0.5mg of FLU were weighed and average weight was calculated. The tablets were crushed and powdered in glass mortar. Quantity of powder equivalent to 10mg ESC and 1mg of FLU was transferred to 100ml volumetric flask, dissolved in sufficient quantity of Water: Methanol(50:50) solvent, sonicated and volume was adjusted up to mark with the solvent to obtain a stock solution 100µg/ml of ESC and 10µg/ml of FLU. This solution was then filtered through Whatmann filter paper. Further dilutions were made from this stock solution to get required concentration. Absorbances of these solutions were measured at appropriate wavelengths, and values were substituted in the respective formula to obtain their respective concentrations. Results of tablet analysis are shown in Table No. 2. The analysis procedure was repeated six times (n=6). Simultaneous equation is used to calculate the concentration of the drugs.

$$C_x = \left(\frac{A_2 a_{y1} - A_1 a_{y2}}{a_{x2} a_{y1} - a_{x1} a_{y2}} \right)$$

$$C_y = \left(\frac{A_1 a_{x2} - A_2 a_{x1}}{a_{x2} a_{y1} - a_{x1} a_{y2}} \right)$$

Where C_x and C_y are concentrations of ESC and FLU respectively in µg/ml in sample solution. A_1 and A_2 are absorbances of the sample solution measured at 238 and 230nm respectively. The absorbances (A_1 and A_2) of

the sample solutions were recorded at 238 and 230nm, respectively and concentration of both components were calculated using above mentioned equation.

Validation^{18, 19}:

The methods were validated with respect to accuracy, linearity, sensitivity, precision and repeatability.

Accuracy (Recovery Test):

To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and 120%). %R.S.D for ESC and FLU, by the method, was found in the range of 0.889. (Table No.2)

Linearity:

The linearity of measurements was evaluated by analyzing different concentration of the standard solution of ESC and FLU. For both the method, the Beer-Lambert's concentration range was found to be 5-25 µg/ml and 0.5-2.5 µg/ml for ESC and FLU respectively.

Sensitivity:

High molar absorptivity and low sandell's sensitivity for the respective method reveals that all these methods are highly sensitive. (Table No.1)

Precision:

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogenous sample under the prescribed conditions. Precision may be considered at three levels: Intermediate (Intraday) precision, reproducibility (Interday precision), repeatability.

1) Intraday Precision:

Solutions containing 10, 15, 20 µg/ml of Escitalopram oxalate and FlupentixolDihydrochloride were analyzed three times on the same day and %R.S.D was calculated.

2) Interday Precision:

Solution containing 10, 15, 20µg/ml of Escitalopram oxalate and FlupentixolDihydrochloride were analyzed different successive days and %R.S.D was calculated.

Repeatability:

Solution containing 15 µg/ml of Escitalopram oxalate and FlupentixolDihydrochloride were analyzed for six times and %R.S.D was calculated. R.S.D was not more than 2%.

Results and Discussion:

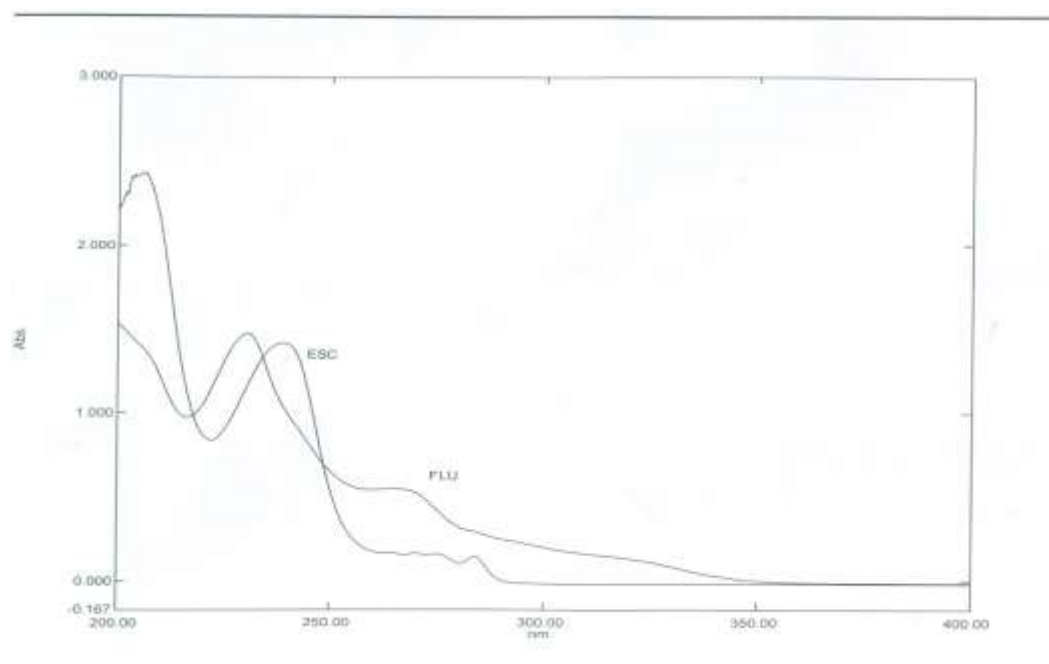
The method discussed in the present work provides a convenient and accurate way for simultaneous analysis of ESC and FLU. In simultaneous equation method, wavelengths selected for analysis were 238nm for ESC and 230nm for FLU. The linearity was observed in the concentration range of 5-25 µg/ml and 0.5-2.5 µg/ml for ESC and FLU respectively. In this method concentration of individual drug present in the tablet sample solution was determined by solving the simultaneous equation at 238nm and 230nm using the respective absorptivity value. Percent label claim for ESC and FLU in tablet analysis, by this method, was found in the range of 94-96%. Accuracy of proposed method was ascertained by recovery studies. The results of validation parameters shown in Table no.1 are satisfactory, indicates the accuracy of proposed method for estimation of ESC and FLU. This method can be employed for routine analysis of these two drugs in combined tablet dosage form. The results obtained for tablets and recovery study is summarized in Table no. 2

Table No: 1 Optical Characteristics and Validation data of Escitalopram oxalate and Flupentixoldihydrochloride.

Parameters	Escitalopram oxalate	Flupentixoldihydrochloride
Working λ (in water:methanol 50:50)	238	230
Molar absorptivity (lit/mole/cm)	21.3	3.14
Sandell's sensitivity (mcg/sq cm/0.001)	0.0194	0.1612
Accuracy (%RSD)	0.889	0.889
Precision(%RSD) Repeatability	1.2	1.2
Linearity	5-25 $\mu\text{g/ml}$	0.5-2.5 $\mu\text{g/ml}$
Regression coefficient(r^2)	0.998 (at 238) 0.998 (at 230)	0.979 (at 238) 0.977 (at 230)

Table No: 2 Result of analysis of tablet Formulation:

Drugs	Label claim (mg)	Amount found	% label claim
ESC	5	4.81	96.2
FLU	0.5	0.47	94.0

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