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NEW RP-HPLC METHOD DEVELOPMENT AND VALIDATION DETERMINATION FOR ESTIMATION OF DULOXETINE HCL IN ENTERIC COATED CAPSULES

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Abstract: A simple, selective, rapid, and precise reverse phase HPLC method has been developed for the simultaneous estimation of duloxetine HCL in enteric coated capsules. An X Terra RP, C-8 column (4.6x150mm) was used for the separation. The mobile phase was acetonitrile: phosphate buffer (65:35%v/v) (Ph5.3) at a flow rate of 1.0 ml/min with detection at 230nm. The retention time was 5.29/minutes. The developed method was validated in term of accuracy, precision, specificity, system suitability, linearity, and robustness. Linearity curve was found to be linear over 20 to 120µg/ml. The proposed method was successfully used to determine the drug content of marketed formulation.

Keywords: Duloxetine HCL, RP-HPLC, Method Validation

Introduction

Duloxetine HCL is chemically, N-methyl-3-napthalen-1-oxy-3-thiophen-2-yl-1-amine. [1] Duloxetine hydrochloride is a newer selective serotonin and norepinephrine reuptake inhibitor (SSNRI) used for major depressive disorders [2] . Duloxetine is not official in any pharmacopoeia. A few methods in literature were reported for the determination of DLX and its key intermediate, desmethyl duloxetine in human serum by HPLC method [3],[4] . Literature reported the characterization of phenolic impurities in Duloxetine HCL samples by MS, NMR, X-ray-analysis [5] and impurities formed by interaction of Duloxetine HCL with various enteric polymers [6] . Our present plan is to develop new, simple, precise, & accurate method for its analysis in formulation, after a detailed study a new RP-HPLC method was decided to be developed and validated. The method was validated according to the ICH (Q_2A 1995) guidelines [7]

Materials and methods

Duloxetine HCL was obtained as gift samples from Dr. Reddys laboratories, Hyderabad. Acetonitrile & methanol were HPLC grade and potassium dihydrogen phosphate was A R grade from Merk chemicals, Mumbai.

Preparation of mobile phase:

Dissolve 27.2 gm of monobasic potassium phosphate in 2000 ml of milli -Q-water, Ph was adjusted to 5.3 by using orthophosphoric acid and Filter through 0.45µm nylon 66 membrane filter.

Mixed above buffer and mobile phase in the ratio 65:35 and degassed in sonicate for about 15 minutes.

Standard preparation:

Transfer about 50mg (equivalent to 44.4 mg of duloxetine) of duloxetin HCL working standard in to 50 ml of volumetric flask, dissolve and dilute to volume with methanol and mixed. Pipette out 1ml of the above solution into 50ml of volumetric flask, dilute to volume with mobile phase.

Test preparation:

Weigh accurately 329 mg duloxetine hydrochloride enteric coated pellets (equivalent to 44.4 mg of duloxetine) transferred it in 50ml volumetric flask, add 25 ml of methanol, shake the flask on rotatory shaker at 200 rpm for 30 minutes and sonicate for 15 minutes with intermediate shaking. Keep the solution on rotatory shaker for 30 minutes at 200 rpm and dilute to volume with methanol. Centrifuge the portion of the above solution at 4000 rpm for 5 minutes. Pipette out 1ml of the above clear solution and transfer it to 50 ml volumetric flask and make up the volume with mobile phase.

System suitability:

Five injection of standard preparation were injected.

Procedure:

Separately inject one blank, two test injection and five injection of standard for system suitability and recorded the areas for major peak.

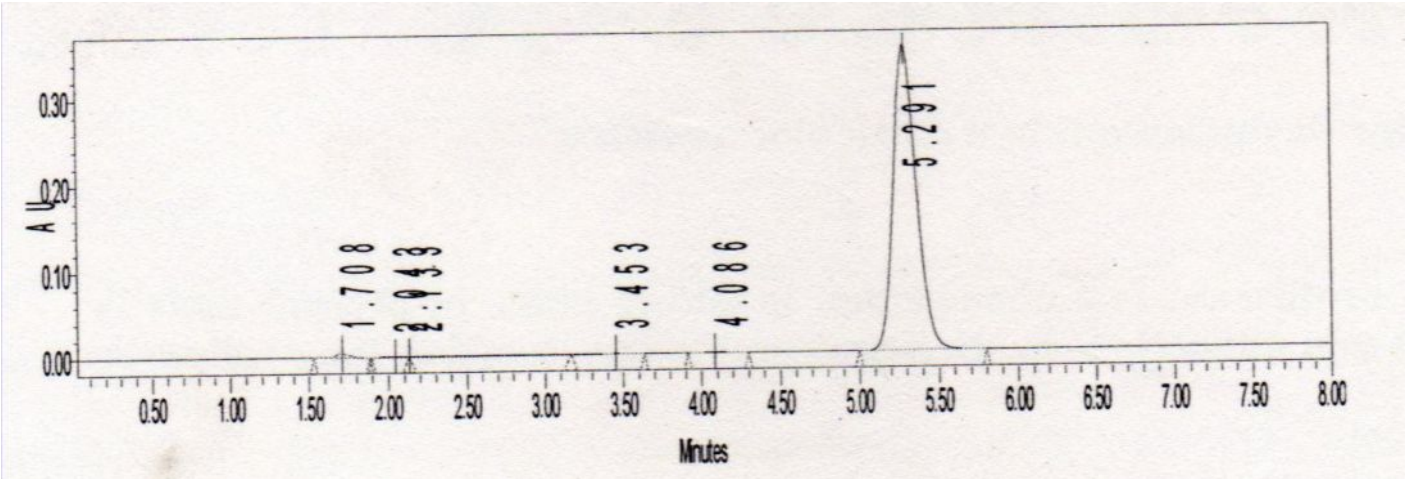
Standard Areas:

1	2	3	4	5	Average	%RSD
3266264	3273081	3282615	3288999	3297622	3281716	0.3

Validation and system suitability parameters

S.No	Parameters	Duloxetin HCL
1	System suitability (%RSD of tailing factor)	1.1
2.	Specificity	No interferences
3	Precision: Repeatability	0.2%
4	Linearity range	20 -120µg/ml
5	Correlation co-efficient	0.9994
6	Accuracy	99.3 - 99.6 %
7	Robustness	Rubustted

Figure-1 Chromatogram for formulation



Result and Discussion

A simple, precision and accuracy HPLC method was developed for the analysis of duloxetin HCL in bulk and enteric coated formulations, consisting of an Acetonitrile: phosphate buffer system (35: 65 % v/v). The chromatographic condition was set at a low rate of 1.0 ml/min with the UV detector at 230 nm. The above method was optimized with a view to develop an assay method for duloxetin HCL

It is evident that the responses for duloxetin HCL was strictly linear in the studied concentration range, which is evident from the RSD values, slop, intercept and correlation. The method worked well in the range from 20 to 160 µg/ ml respectively which suggests full capacity for the quantification of duloxetin.

The data obtained from the precision experiment. The RSD value for precision was 0.4 indicating that method was sufficiently precise.

Percentage of recovery was calculated from 25% to 150% by spiked method. The excellent recovery was made at each added concentration.

There is allowable variation in flow rate, temperature, Ph, and mobile phase composition which indicate that method is robust enough.

The low RSD value for percent assay of test preparation revealed that the proposed method is rugged. The chromatogram of sample showed a single peak at the retention time of duloxetin indicating that there is no interference of the excipients in the formulation.

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