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STABILITY INDICATING DISSOLUTION ANALYTICAL METHOD VALIDATION OF VENLAFAXINE IN PELLETS BY UV-SPECTROPHOTOMETER

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Abstract
To develop & validate new dissolution analytical method for venlafaxine in pellets by uv-spectrophotometer Solubility determination of venlafaxine in 0.1N HCl, Determine the absorption maxima of the drug in UV-Visible region in 0.1N HCl , Develop a new dissolution analytical method for venlafaxine in pellets by uv-spectrophotometer ,Validate the developed method as per ICH guidelines. The current good manufacturing practices (CGMP) and the Food Drug Administration (FDA) guidelines insist for adoption of sound methods of analysis with greater sensitivity and reproducibility. Therefore, the complexity of problems encountered in pharmaceutical analysis with the importance of achieving the selectivity, speed, low cost, simplicity, sensitivity, specificity, precision and accuracy in estimation of drugs.

Keywords: venlafaxine, UV-spectrophotometer, HCl, CGMP, FDA.

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Introduction

Analytical chemistry

Analytical chemistry is a scientific discipline used to study the chemical composition, structure and behaviour of matter. The purposes of chemical analysis are together and interpret chemical information that will be of value to society in a wide range of contexts. Quality control in manufacturing industries, the monitoring of clinical and environmental samples, the assaying of geological specimens, and the support of fundamental and applied research are the principal applications. Analytical chemistry involves the application of a range of techniques and methodologies to obtain and assess qualitative, quantitative and structural information on the nature of matter.

- Qualitative analysis is the identification of elements, species and/or compounds present in sample.
- Quantitative analysis is the determination of the absolute or relative amounts of elements, species or compounds present in sample.

Structural analysis is the determination of the spatial arrangement of atoms in an element or molecule or the identification of characteristic groups of atoms (functional groups). An element, species or compound that is the subject of analysis is known as analyte. The remainder of the material or sample of which the analyte(s) form(s) a part is known as the matrix.

The gathering and interpretation of qualitative, quantitative and structural information is essential to many aspects of human end eavour, both terrestrial and extra-terrestrials. The maintenance of an improvement in the quality of life throughout the world and the management of resources heavily on the information provided by chemical analysis. Manufacturing industries use analytical data to monitor the quality of raw materials, intermediates and finished products. Progress and research in many areas is dependent on establishing the chemical composition of man-made or natural materials, and the monitoring of toxic substances in the environment is of ever increasing importance. Studies of biological and other complex systems are supported by the collection of large amounts of analytical data. Analytical data are required in a wide range of disciplines and situations that include not just chemistry and most other sciences, from biology to zoology, butte arts, such as painting and sculpture, and archaeology. Space exploration and clinical diagnosis are two quite desperate areas in which analytical data is vital. Important areas of application include the following.

Quality control (QC) in many manufacturing industries, the chemical composition of raw materials, intermediates and finished products needs to be monitored to ensure satisfactory quality and consistency. Virtually all consumer products from automobiles to

clothing, pharmaceuticals and foodstuffs, electrical goods, sports equipment and horticultural products rely, in part, on chemical analysis. The food, pharmaceutical and water industries in particular have stringent requirements backed by legislation for major components and permitted levels of impurities or contaminants. The electronic industry needs analyses at ultra-trace levels (parts per billion) in relation to the manufacture of semi-conductor materials. Automated, computer-controlled procedures for process-stream analysis are employed in some industries.
Monitoring and control of pollutants The presence of toxic heavy metals (e.g., lead, cadmium and mercury), organic chemicals (e.g., polychlorinated biphenyls and detergents) and vehicle exhaust gases (oxides of carbon, nitrogen and sulphur, and hydrocarbons) in the environment are health hazards that need to be monitored by sensitive and accurate methods of analysis, and remedial action taken. Major sources of pollution are gaseous, solid and liquid wastes that are discharged or dumped from industrial sites, and vehicle exhaust gase

Aim

To develop & validate new dissolution analytical method for venlafaxine in pellets by uv-spectrophotometer.

Plan of Work

- Solubility determination of venlafaxine in 0.1N HCl
- Determine the absorption maxima of the drug in UV-Visible region in 0.1N HCl.
- Develop a new dissolution analytical method for venlafaxine in pellets by uv-spectrophotometer
- Validate the developed method as per ICH guidelines.

This thesis work comprises of,
1. Method of analysis.
2. Validation of Assay method (To be done by using following parameters):
    1. Specificity
    2. System suitability
    3. Linearity
    4. Precision
        1.1 System precision
        1.2 Method precision
    5. Accuracy
    6. Robustness
    7. Ruggedness
    8. Solution stability

Materials and Methods

Method of analysis

The following standards, samples and reagents are used for validation study

1. Venlafaxine working standard (Batch no: SCWS09001), Purity: 99.91
2. Venlafaxine pellets 65.0%w/w test sample (Batch no: SEPCB09001)

Reagents

1. Hydrochloric acid; Lot no: 9713 6912-5; Make: Qualigens.
2. DM water.

Instrument Used

Shimadzu UV-2450 Spectrophotometer contains

1. Both reference and sample cells.
2. Output signals and readings were monitored by UV-probe 2.33 version software.

Dissolution conditions

Apparatus : USP Apparatus II (Paddle type)
Sampling interval : 30min
Medium : 900ml of 0.1N HCl
RPM : 100
Temperature : $37^0C \pm 0.5^0C$.

Results & Discussion

Validation of Analytical Method

1. Specificity

Sequence for specificity

S.No.	Sample name	Number of Readings
1	Blank	1
2	Placebo solution	1
3	Standard preparation	1
4	Sample preparation	1

Linearity

Sequence for linearity

S.No.	Sample name	Number of Readings
1	Standard solution	1
2	40% Linearity solution	1
3	60%Linearity solution	1
4	80% Linearity solution	1
5	100% Linearity	1
6	120% Linearity	1

Observation

Concentratio	40%	60%	800	100	120
absorbance	0.18	0.28	0.377	0.471	0.565

Acceptance criteria

- Correlation coefficient should be not less than 0.99.
- % y-intercept should be between ±5.0.

2. Precision

Sequence of injections

S.No.	Sample name	Number of Readings
1	Standard preparation	6

Method precision

Sequence of injections

S.No.	Sample name	Number of Readings
1	Standard preparation	6
2	Sample preparation 1	1
3	Sample preparation 2	1
4	Sample preparation 3	1
5	Sample preparation 4	1

6	Sample preparation 5	1
7	Sample preparation 6	1

Accuracy

Sequence for accuracy

S.No.	Sample name		Number of
1	Standard preparation		1
2	Accuracy 50% solution	Preparation-	1
		Preparation-	1
		Preparation-	1
3	Accuracy 100% solution	Preparation-	1
		Preparation-	1
		Preparation-	1
4	Accuracy 150% solution	Preparation-	1
		Preparation-	1
		Preparation-	1

Robustness

Deliberately modified chromatographic conditions

Deliberately modify the actual test conditions specified under the method like buffer preparation.

S.No.	Dissolution media	Actual volume of HCl/lit	Modified volum of HCl/lit-1	Modified volum of HCl/lit-2
1	0.1N HCl	8.5	8.3	8.7

Filter variability

Determine the Dissolution of Venlafaxine pellets by using different filters.

S.No.	Actual method	Different Filters	
		Experiment-	Experiment-
1	Whatman Filter	As it is	0.45µ Filter

Ruggedness

Sequence for Intermediate precision

S.No.	Sample name	Number of Readings
1	Standard preparation	1
2	Sample preparation 1	1
3	Sample preparation 2	1
4	Sample preparation 3	1
5	Sample preparation 4	1
6	Sample preparation 5	1
7	Sample preparation 6	1

Chemist- II, Day- II

Test sample results

Sample No.	Absorbance	%Dissolution
STD	0.472	
1	0.510	101.66
2	0.508	101.03
3	0.511	101.55
4	0.511	101.70
5	0.510	101.54
6	0.512	102.06
Average		101.59
standard Deviation		0.335
%RSD		0.329

Overall %RSD for method precision

S.No	%Dissolution
1	102.73
2	102.90
3	102.01
4	102.57
5	102.21
6	102.53
7	101.66
8	101.03
9	101.55
10	101.70
11	101.54
12	102.06
Average	102.04
standard Deviation	0.567
%RSD	0.556

Acceptance criteria

- The %RSD for six dissolution values should not be more than 5.0.
- The overall %RSD for the dissolution values obtained in method precision and the intermediate precision should not be more than 5.0.

Solution Stability

S. No	Time interval	%Dissolution (RT)	%Dissolution difference (RT)	%Dissolution (2-8^{0}C)	%Dissolution difference (2-8^{0}C)
1	Ineti	101.93	-	101.93	-
2	4th	106.90	4.88	106.40	4.39

Acceptance criteria

The percentage difference in Dissoltion from initial and at each interval should not be more than ±2.0.

Conclusion

The pharmaceutical analyst plays a major rule in assuring identity, safety, efficacy, purity, and quality of a drug product. The need for pharmaceutical analysis is driven largely by regulatory requirements. The commonly used tests of pharmaceutical analysis generally entail compendia testing method development, setting specifications, and method validation. Analytical testing is one of the more interesting ways for scientists to take part in quality process by providing actual data on the identity, content and purity of the drug products. Pharmaceutical analysis occupies a pivotal role in statuary certification of drugs and their formulations either by the industry or by

the regulatory authorities. In industry, the quality assurance and quality control departments play major role in bringing out a safe and effective drug or dosage form. The current good manufacturing practices (CGMP) and the Food Drug Administration (FDA) guidelines insist for adoption of sound methods of analysis with greater sensitivity and reproducibility. Therefore, the complexity of problems encountered in pharmaceutical analysis with the importance of achieving the selectivity, speed, low cost, simplicity, sensitivity, specificity, precision and accuracy in estimation of drugs.

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