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VALIDATION OF SOP OF DISSOLUTION APPARATUS USING ACELOFENAC TABLETS

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ABSTRACT A dissolution method was validated for evaluation of the dissolution behavior of tablet dosage form containing aceclofenac as there was no official method available. Four different commercially available products were selected for this study.The method was validated according to International Conference on Harmonisation (ICH) guidelines which include accuracy, precision, specificity, linearity, and analytical range. In addition, stability and solubility of the drug in different media i.e., water, 0.1 N HCl, acetate buffer and phosphate buffer of different pH were studied. Based on this, dissolution medium containing 0.02 M phosphate buffer, pH 6.8, was found suitable to ensure sink conditions and chemical stability for both the drugs. The established dissolution conditions were 900 ml dissolution medium at temperature 37 ± 0.5°C, using USP apparatus II at stirring rate of 50 rpm for 40 min. The corresponding dissolution profiles were constructed and all the selected brands showed more than 80% drug release within 30 min. The in vitro release profiles were compared for the similarity using the f2 test. Thus, the proposed dissolution method can be applied successfully for the quality control of aceclofenac tablets.

KEYWORDS : Acelofenac, Dissolution, Solubility

INTRODUCTION : The dissolution test is a simple and useful in vitro tool that can provide valuable information about drug release similarity among different batches and brands. It describes about manufacturing reproducibility, product performance similarity and biological availability of drug from its formulation. Therefore, it is considered as one of the most quality control test of solid pharmaceutical dosage forms.Chemically, Aceclofenac (ACE), 2-{2-[2-(2,6 Dichlorophenyl) aminophenyl]acetyl}oxyacetic acid is a non steroidal anti-inflammatory drug (NSAID) indicated for symptomatic treatment of pain and inflammation with a reduced side effect profile, especially gastro intestinal events that are frequently associated with NSAID therapy. It is practically insoluble in water and belongs to Biopharmaceutics classification system (BCS) class II (low solubility, high permeability).Dissolution testing of formulations containing poorly soluble drugs has experienced increasing interest in recent years for finding proper conditions for the routine quality control.ACE is official in BP4. A number of methods have been reported for the analysis of ACE either by UV or HPLC. The literature search revealed lack of validated dissolution test for the ACE tablets. Therefore, the method development and validation of dissolution test for the tablets of ACE were developed.

MATERIALS AND METHODS

All experiments were performed by pharmaceutical grade ACE (Aurobindo pharmaceuticals Ltd, Hyderabad), analytical grade reagents and solvents. Buffer solutions were prepared by double distilled water. All dilutions were performed in standard volumetric flasks. Solvents and solutions were filtered through 0.45 µm nylon filters before use. The pharmaceutical preparations containing 100 mg ACE were procured from local drug stores.

Solubility Studies

Solubility data was used as the basis for the selection of the best medium for dissolution of ACE tablets. For equilibrium solubility studies, excess of the drug, ACE was placed in 25 ml beakers containing different media: distilled water, 0.1 N HCl (pH 1.2), pH 4.5 acetate buffer and phosphate buffer of pH 6.8, pH 7.2 and pH 7.4. The samples were gently rotated in water bath shaker at 37.0 ± 0.5 ºC for 24 h. An aliquot (2 ml) was removed from each beaker after 12 h and 24 h and filtered using 0.45 µm syringe filter. 1 ml of the filtered sample was diluted with corresponding medium and analyzed spectrophotometrically in triplicate to determine the absorbance at their respective λmax. The amount of drug dissolved was calculated using the calibration curve.

Dissolution method development and validation

One tablet was placed in each of the six vessels of the dissolution apparatus USP type II (Tablet dissolution tester, USP model: TDT- 06P, Electrolabs, India), containing 900 ml of 0.02 M Phosphate buffer (pH 6.8), preheated at 37 ± 0.5°C and the dissolution medium was stirred at 50 rpm. Aliquots of the dissolution medium (5 ml) were withdrawn at 5, 10, 20, 30 and 40 min and filtered, discarding the first portions of the filtrate; 2 ml of the filtrates were transferred to 50 ml volumetric flasks and made up to the mark with buffer. The amount of drug dissolved was determined by UV using the simultaneous equation method.

Validation

The dissolution method was validated for precision and robustness as per the ICH guidelines. The interday precision was determined by analysis of two sets of six tablets each, from the same lot on two different days. The robustness of the dissolution method was established by performing dissolution at two different paddle speed (50 and 75 rpm).

Data analysis

The dissolution profiles were analyzed by similarity factor. The similarity factor (f2) is a logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent (%) dissolution between the two curves. The following equation was used to calculate the similarity factor f2. Where, n is the number of time points, Rt is the dissolution value of reference product at time t and Tt is the dissolution value for the test product at time t. According to FDA, the dissolution profiles are found to be similar if f2 is between 50 and 100.

RESULT AND DISCUSSION

Dissolution method development and validation

The experimental results revealed that the dissolution rate of ACE increased with time irrespective of the paddle speed. More than 80% of the drug was released within 30 min.The dissolution method precision was evaluated by performing inter day precision and all the four brands showed % RSD less than 2%. Thus, the method was precise. The robustness of the dissolution method was performed employing different paddle speed of 50 and 75 rpm. As there was not much difference in the release rates, the method was found to be robust.

Table: Solubility of Aceclofenac

Solvent	Solubility ± SD (µg/ml)
	ACE
Distilled water	0.18 ± 0.2
0.1 N HCl	0.045 ± 0.1
Acetate buffer pH 4.5	5.2 ± 0.3
Phosphate buffer pH 6.8	9.6 ± 0.1
Phosphate buffer pH 7.2	6.2 ± 0.3
Phosphate buffer pH 7.4	6.7 ± 0.1

Table : Absorptivities of Aceclofenac

Absorptivity	ACE	
	At 243 nm	At 273 nm
Mean ± SD	183.89	248.30
	183.88	248.35
	183.93	248.31
	183.90 ± 0.02	248.32 ± 0.02

Table : Accuracy and Precision Data for ACE in Marketed Formulations

Brand	% Recovery ± SD	Repeatability (%RSD)	Intra Day Precision (%RSD)	Inter Day Precision (%RSD)
			Lab1 Lab2	Day1 Day2
ACE				
A	99.21 ± 0.26	0.5	0.5 0.4	0.5 0.3
B	99.64 ± 0.41	0.5	0.5 0.4	0.5 0.4
C	98.56 ± 0.58	0.4	0.4 0.5	0.4 0.4
D	99.71 ± 0.51	0.4	0.4 0.4	0.4 0.3

CONCLUSION

Dissolution is a characterization test commonly used by the pharmaceutical industry to guide formulation design and control product quality. It is used as a quality control tool. The analytical method for the aceclofenac developed was UV spectrophotometric method involving the simultaneous equation method for the simultaneous estimation of ACE. The wavelength employed in this method was 273 nm (λmax of ACE). The method was validated for various parameters like linearity, accuracy, precision and specificity. All the parameters were found to be under the acceptance criteria. The *in vitro* dissolution profile was obtained using 900 ml of dissolution medium containing 0.2 M phosphate buffer pH 6.8 maintained at 37º ± 0.5ºC with paddle apparatus at 50 rpm. More than 85% of the drug, ACE were released within 30 min. The drug release rates were compared using the similarity factor and were found similar. Thus, the dissolution method developed was precise, accurate and reproducible and can be employed as a quality control method.

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