COMPARATIVE DISSOLUTION PROTOCOL/REPORT

COMPARATIVE DISSOLUTION FOR PARACETAMOL 500mg TABLETS

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XX PHARMACEUTICALS LIMITED

117 Adams Street, Brooklyn, NY 11201, USA

Protocol Approval

Prepared By:

Name: Rex Barrett

Designation: Asst. Manager, QC

Department: Quality Assurance

Signature & Date:

Checked By:

Name: Caleb Hines

Designation: Manager, Quality Control

Department: Quality Assurance

Signature & Date:

Agreed By:

Name: Milton Alvarado

Designation: Manager, Plant

Department: FAD

Signature & Date:

Approved By:

Name: Joanna Warner

Designation: Manager, Quality Assurance

Department: Quality Assurance

Signature & Date:

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2. INTRODUCTION:

Dissolution testing is an in vitro technique of great importance in formulation and development of pharmaceutical dosage forms, as it can be used as a substitute for in vivo studies under strictly defined & specified conditions. Dissolution testing is described as ensuring adequate & reproducible bioavailability without recourse to routine in-vivo testing. On some occasions, this may be achieved by dissolution testing of a particular product for which in vitro-in vivo correlation has been demonstrated.

3. OBJECTIVE:

The objective is to conduct the comparative dissolution studies of Ridenapro formulation of Paracetamol 500mg Tablets & innovator or leading marketed brand. Dissolution testing in different dissolution media viz., pH 1.2, pH 4.5 & pH 6.8 is conducted for 12 tablets from both brands for 60 min. by using dissolution testing paddle apparatus.

A more common objective of dissolution testing is to obtain information about the drug release characteristics of a particular formulation or batch of product under standardized in vitro testing conditions.

4. RESPOSIBILITY:

4.1 It is the responsibility of validation officer to perform the comparative dissolution as per regulatory guideline.

4.2 The Manager, QC, should ensure that methods of analysis are available & that the equipment to be used for analysis is properly working & calibrated & chemicals used for analysis are available.

4.3 The Manager, QA should ensure that the comparative dissolution should meet the acceptance criteria & maintain records for further activity.

5. METHODOLOGY:

5.1 Equipments

List down equipments used with ID and Calibration Status

5.2 Chemicals

List down chemicals used with ID and Calibration Status

5.3 Glasswares

List down Glasswares used with ID and Calibration Status

5.4 Documents Used :-

Standard operating procedure	:	

Calibration documents	:	

5.5 Working Standard Used :

Write details for working standard used

5.6 Sample used for Dissolution :-

Name of sample	:		
Manufactured By	:		
Batch Number	:		
Manufacturing date	:		
Expiry date	:		

5.7 Reference sample used for Dissolution :-

5.8 Method of Analysis:

5.8.1 Dissolution Media:

· Preparation of Buffer pH 1.2:

Transfer accurately 8.5mL of hydrochloric acid into a 1000 mL water & mix. Adjust pH 1.2 with hydrochloric acid.

· Preparation of Phosphate Buffer pH 4.5:

Dissolve 13.6 g of sodium acetate and 6 mL of glacial acetic acid in sufficient water to produce 1000 mL. Adjust the pH 4.5.

· Preparation of Phosphate Buffer pH 6.8:

Dissolve 5.5 g of sodium dihydrogen phosphate & 9.0 g of sodium chloride in 1000 mL of water. Adjust the pH 6.8 with sodium hydroxide solution.

5.8.2 Dissolution Method:

Medium : 900 mL

Apparatus : II (Paddle)

Speed : 50 RPM

Temperature : 37.0C ± 0.50C

Standard Preparation:

Weigh XX mg of Paracetamol WS 100mL volumetric flasks, add 70mL of dissolution medium to dissolve & dilute with same to volume. Filter through 0.45µ filter. Measure the absorbance at XX nm.

Sample Preparation:

Place 900 mL of dissolution medium maintained at 37 ± 0.5°C in 6 dissolution vessels separately & fix in the tablet dissolution bath. fix the paddle to the shaft & bring it into the position. Place 1 tablet each into 6 dissolution vessels. Operate the instrument at 50 RPM for 60 min. Withdraw 5 mL of the medium at the interval of 10, 15, 20, 30, 45 & 60 minutes & replace with same dissolution medium with same volume at each interval. Filter through 0.45µ filter. Measure the absorbance at XXnm.

Calculation: Calculate the percentage of labeled amount dissolved:

=At/As×Ws/100×V/L× P

Where,

At = Absorbance of Sample solution

As = Absorbance of Standard solution

L = Label claim

V = Volume of medium

P = Purity of standard

6. DATA ANALYSIS:

6.1 Two scenarios for comparing the profiles obtained from multipoint dissolution are operative: 6.1.1 If both the test and reference product show more than 85% dissolution within 15 minutes, the profiles are considered similar (no calculations required). If not, see the next point.

6.1.2 Calculate the f2 value. If f2 ≥ 50, the profiles are normally regarded similar such that further in vivo studies are not necessary. Note that only one measurement should be considered after 85% dissolution of both products has occurred and excluding point zero.

6.2 The difference factor ($f1$) calculates the percent (%) difference between the two curves at each time point & is a measurement of the relative error between the two curves:

$$f_1 = \left\{\left[\sum_{t=1} n\,|R_t - T_t|\right] / \left[\sum_{t=1} nRt\right]\right\} \cdot 100$$

6.3 The similarity factor (f2) is a logarithmic reciprocal square root transformation of the sum of squared errors, and is a measurement of the similarity in the percentage (%) dissolution between the two curves.

$$f_2 = 50 \cdot log\left\{\left[1 + (1/n)\sum_{t=1}^{n} n\,(R_t - T_t)^2\right]^{-0.5} \cdot 100\right\}$$

Where,

n = The number of time points Rt = The dissolution value of the reference batch at time t Tt = The dissolution value of the test batch at time t.

6.4 A specific procedure to determine difference and similarity factor is as follows:

6.4.1 Determine the dissolution profile of two products, i.e. of the test and reference products (using 12 units each).

6.4.2 For f2 calculations a minimum of three time points (excluding point zero) must be used, and only one measurement included after 85 % dissolution of both products has occurred.

6.4.3 For curves to be considered similar, f2 values should be close to 100. Generally, f2 values greater than 50 (50 to 100) ensure sameness or equivalence of the two curves and, thus, of the performance of the test and reference products.

6.5 This model-independent method is most suitable for dissolution profile comparisons when three to four or more dissolution time points are available. The following recommendations should also be considered:

6.5.1 The dissolution measurements of the test and reference batches should be made under exactly the same conditions. The dissolution time points for both profiles should be the same (e.g. 10, 15, 20, 30, 45, 60 minutes, etc.). For rapidly dissolving products (profiles reaching 85 % at 30 minutes) the minimum time points are 10, 15, 20 and 30 minutes.

6.5.2 Only one measurement should be considered after 85 % dissolution of both products have occurred.

6.5.3 To allow use of mean data, the percent coefficient of variation (CV) at the earlier time points (e.g. 15 minutes) should not be more than 20 %, and at other time points should not be more than 10 %.

7. SIMILARITY FACTOR & DIFFERENCE FACTOR CALCULATION:

7.1 : Dissolution Medium pH 1.2

Time	R_t	T_t	$(R_t - T_t)$	$(R_t - T_t)^2$	Sum (R_t-T_t)	
0 min					Sum $(R_t - T_t)^2$	
10 min					Sum R_t	
15 min					Number of Points	
20 min					Difference factor f_1	
30 min					Similarity factor f_2	
45 min						
60 min						

7.2 : Dissolution Medium pH 4.5

Time	R_t	T_t	$(R_t - T_t)$	$(R_t - T_t)^2$	Sum (R_t-T_t)	
0 min					Sum $(R_t - T_t)^2$	
10 min					Sum R_t	
15 min					Number of Points	
20 min					Difference factor f_1	
30 min					Similarity factor f_2	
45 min						
60 min						

7.3 : Dissolution Medium pH 6.8

Time	R_t	T_t	$(R_t - T_t)$	$(R_t - T_t)^2$	Sum (R_t-T_t)	

0 min					**Sum ($R_t - T_t)^2$**	
10 min					**Sum R_t**	
15 min					**Number of Points**	
20 min					**Difference factor f_1**	
30 min					**Similarity factor f_2**	
45 min						
60 min						

8. SUMMARY:

Disso. Medium	**Manufactured by**	**% Drug Release**						**Factor Calculation**	
		10 min	15 min	20 min	30 min	45 min	60 min	*f_1*	*f_2*
pH 1.2									
pH 4.5									
pH 6.8									

9. <u>CONCLUSIONS:</u>