Quest Journals
Journal of Research in Pharmaceutical Science
Volume 9 ~ Issue 6 (2023) pp: 10-14
ISSN(Online) : 2347-2995
www.questjournals.org

Research Paper

Invitro equivalence Study on the Dissolution profiles of Etoricoxib tablets using Biopharmaceutical Classification System Criteria.

Amit Sah*: Quality Control Manager, S.R. Drug Laboratories Pvt Ltd., Kathmandu, Nepal*
Sagar Shrestha*: Sr. Quality Control Officer, S.R. Drug Laboratories Pvt Ltd., Kathmandu, Nepal*
Sangam Shahi*: Sr. Quality Control Officer, S.R. Drug Laboratories Pvt Ltd., Kathmandu, Nepal*

Abstract:
Multiple pharmaceutical products need to conform to the same appropriate standards of quality, efficacy, and safety as those required of the innovator's product. For class BCS II drugs, like Etoricoxib, it is very important to perform an invitro equivalence dissolution test as drug dissolution may be a rate-limiting step in the drug absorption process for different formulations in physiological conditions. In the present work, the dissolution profiles of formulated products have been compared to Innovator product under the same test conditions in order to calculate the similarity and dissimilarity factor. The dissolution study was conducted using the following media: buffer pH 6.8, 4.5, and 0.1 M HCl. For quantitative analysis, UV/Vis spectrophotometry turned into use due to the fact this technique has been thoroughly validated. The results show that both the test product and innovator product show a similar response in selective dissolution media which concludes the test product is identical to the innovator product.

Keywords: *BCS, Etoricoxib, Innovator Product, Dissolution Study, UV/Vis Spectrophotometry.*

***R**eceived 02 June, 2023; **R**evised 10 June, 2023; **A**ccepted 13 June, 2023 © The author(s) 2023.*
P**ublished with open access at **www.questjournals.org

I. Introduction

Etoricoxib is a nonsteroidal anti-inflammatory drug, used to relieve pain and inflammation by selectively inhibiting isoform 2 of cyclo-oxygenase enzyme (COX-2), preventing the production of prostaglandins from arachidonic acid[1]. It has a higher COX-1 to COX-2 selectivity ratio than the other COX-2-selective NSAIDs rofecoxib, valdecoxib, or celecoxib[2]. Current therapeutic indications are the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, chronic low back pain, acute pain, and gout[3]. According to the Biopharmaceutical Classification System (BCS), Etoricoxib had been classified as a class II drug (low solubility and high permeability); therefore, drug dissolution can be a rate-restricting step inside the drug absorption process[4].

At present, the multisource pharmaceutical products that belong to the BCS class II require an invitro equivalence dissolution test to conform to the same appropriate standards of quality, efficacy, and safety[5]. It is frequently essential to acquire records at more than one-time factor to thoroughly characterize the invitro overall performance of the drug product extra exactly than the factor estimate approach[6]. The resulting dissolution profiles of the product under different dissolution mediums (pH buffer) can then be compared using model-independent or model-dependent methods. The model-independent similarity factor (f2) method is an enormously easy and extensively general approach for dissolution profiles. Many regulatory authorities require the use of the f2 take a look at for this purpose[7].

The study was set up to evaluate and compare the in-vitro dissolution profiles of formulated tablets of Etoricoxib tablets with the innovator that is available in the Nepali market with BCS criteria using UV/Vis spectrophotometry for quantitative drug analysis.

II. Materials and Methods

All materials used in these investigations were of the highest purity available. They included standard grade Etoricoxib with a purity of 99.90. The active ingredients are approved with a comparison of Etoricoxib IPRS with an ID IPRS/65/13. All other solvents and reagents were of analytical grade or equivalent. The internal product solid tablets dosage formulations of the drug were compared with the innovator market sample. The twelve tablets were individually weighed before use in the dissolution studies, general information on these drugs is reported in Table.

For chemicals details:

Name	:	Grade	Manufacturer	Mfg Date	Expiry Date
Etoricoxib	:	Working standard	Seutic Labs Pvt Ltd.	Feb'22	Jan'25
Hydrochloric Acid	:	AR grade	Loba Chemi Pvt Ltd.	Sep'21	Aug'26
Sodium Acetate Trihydrate	:	AR grade	Sisco Research Laboratories Pvt. Ltd.	Apr'19	Mar'24
Monobasic Sodium Phosphate	:	AR grade	Merck Specialities Pvt. Ltd.	Dec'19	Nov'24
Sodium Hydroxide	:	AR grade	Loba Chemi Pvt. Ltd.	May'21	Exp'26

For standard details:

Name of standard	**Reference No.**	**% Purity**	**%Lod**	**Validity**
Etoricoxib	WS-108/018/555/79	100.16 (ODB)	0.18	01/12/024

SN	**Product Details**	**Test Product**	**Reference Product**
1.	Generic Name	Etoricoxib Tablets IP	
2.	Brand Name	Etoricoxib 90 FCT	Intacoxia-90
3.	Batch No.	TT-001/90	EFT-022301
4.	Mfg Date	Jan 2023	Feb 2023
5.	Expiry Date	Dec 2024	Jan 2025
6.	Manufactured By	SR Drug Laboratories Pvt Ltd	Intas Pharmaceuticals Ltd.
7.	Storage Condition	Store protected from light and moisture, at a temperature not exceeding 30 °C	

Equipment used	Make	Calibration Due
Analytical weighing balance	Denver	Nov'23
	Shimadzu	
Dissolution Apparatus	Electrolab	Nov'23
UV Spectrophotometer	Agilent	Apr'24
pH meter	Spectra	Daily Calibration

Dissolution:

Medium:	0.1 N HCl, Acetate Buffer 4.5, Phosphate Buffer 6.8	Volume:	900 ml
Apparatus:	Paddle	Rpm:	75
Time:	5,10,15,20,30,45,60 minutes	Temperature:	37 ± 0.5 °C

Preparation of 0.1 N HCl
Dissolve 80 ml of Conc. HCl in 1000 ml of water.

Preparation of Acetate Buffer pH 4.5:
Weigh 27.20 g of Sodium Acetate Trihydrate into a one-liter volumetric flask. Add 800 mL of deionized water. Mix and dissolve. Bring the pH down to 4.5 with Glacial Acetic Acid.

Preparation of Phosphate Buffer pH 6.8:
Dissolve 6.8 g of monobasic potassium phosphate in 1 liter of water and adjust with 1 N sodium hydroxide to a pH of 6.8.
These media were selected based on WHO TRS 1003 Annex 6: Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability and the FDA Guidance for Industry and the need to meet the criteria for biowaiver (FDA guidelines, 2000).

Dissolution Procedure:
Place the stated volume of dissolution medium in the vessel; assemble the apparatus, maintain the above parameters, and allow to equilibrate at 37 ± 0.5 °C. Individually weigh the 12 tablets and place them in each of the 12 vessels and immediately operate the apparatus at the rate specified within the time interval. Withdraw 10

ml of the medium at specified time intervals from the zone midway between the surface of the dissolution medium and the top of the rotating paddle, not less than 1 cm from the vessel wall, and filter through Whatmann no.1 filter paper. Immediately replace 10 ml of the medium maintained at 37 ± 0.5 °C in each vessel. Dilute 1 ml of the filtrate to 25 ml with the medium.

Measure the absorbance of both the standard and sample solutions at about 240 nm using dissolution medium as blank. Calculate the % of Etoricoxib as follows:

% of Etoricoxib released

$$= \frac{\text{Abs.of Sample}}{\text{Abs.of Standard}} \times \frac{\text{Weight of Standard}}{\text{Weight of Sample}} \times \frac{\text{Sample Dilution}}{\text{Standard Dilution}} \times \frac{\text{Standard Potency}}{100} \times \frac{1}{\text{label Claim}} \times 100$$

Data Analysis

If both the test and the comparator product show more than 85% dissolution in 15 minutes the profiles are considered similar no calculation is required. The similarity of the resulting comparative dissolution profiles should be calculated using the following equation that defines a similarity factor.

F2 value between 50 and 100 suggests that the two dissolution profile are similar.

A maximum of one point should be considered after 85% dissolution of the reference product has been reached.

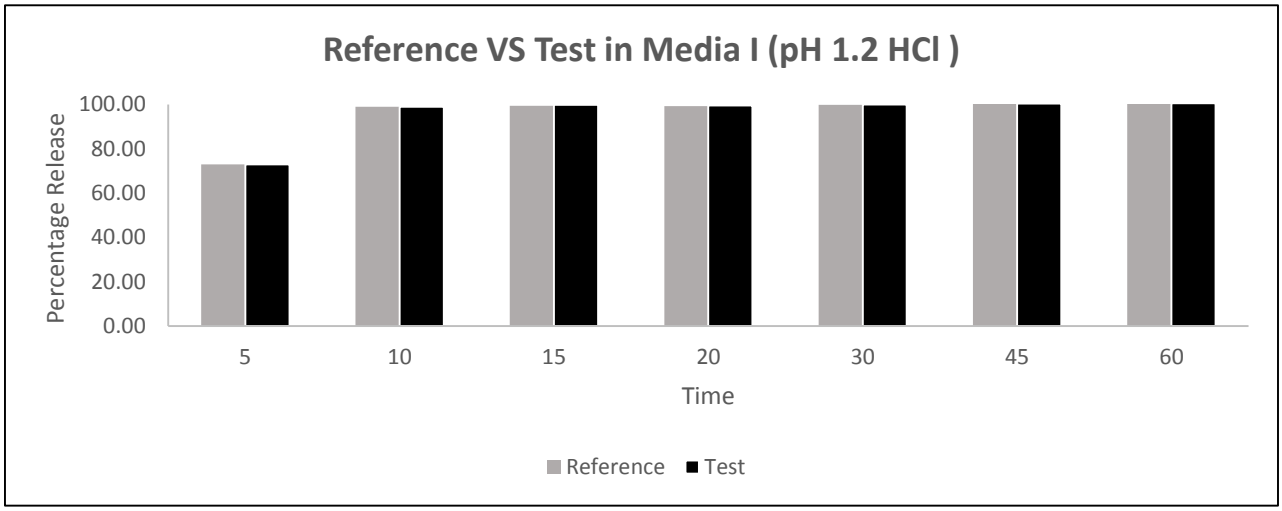
In case where 85% dissolution cannot be reached owing to poor solubility of the API of the release mechanism of the dosage form, the dissolution should be conducted until an asymptote has been reached.

At least 12 units should be used for the determination of each profile. Mean dissolution values can be used to estimate the similarity factor, f2. To use mean data the percentage coefficient of variation at initial points should not be more than 20% and at other time points should be not more than 10%.

III. Results and Discussion

In Acid Stage (0.1 N HCl)

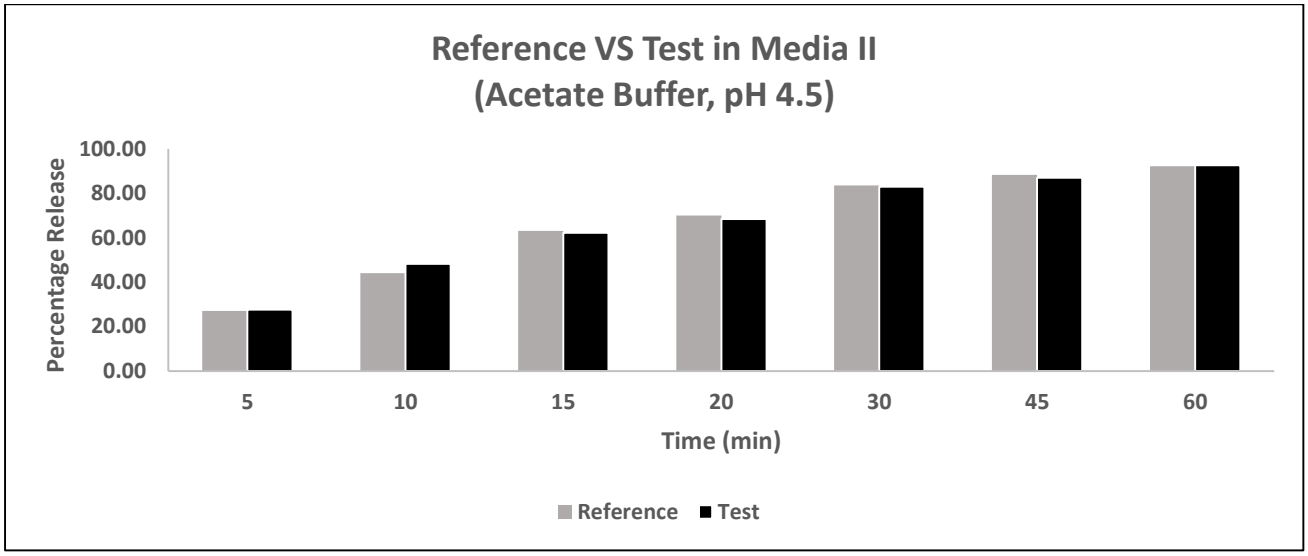
	% Release	
Sampling Time point (min)	Referene Product (R_t)	Test Product (T_t)
5	73.01	72.99
10	98.86	98.91
15	99.32	99.77
20	99.27	99.56
30	99.80	99.87
45	100.60	100.33
60	100.80	100.45
No. of time points	6.00	



In Acetate buffer, pH 4.5:

	% Release	
Sampling Timepoint (min)	Reference Product (R_t)	Test Product (T_t)
5	27.01	27.62
10	44.04	48.22
15	63.08	62.24

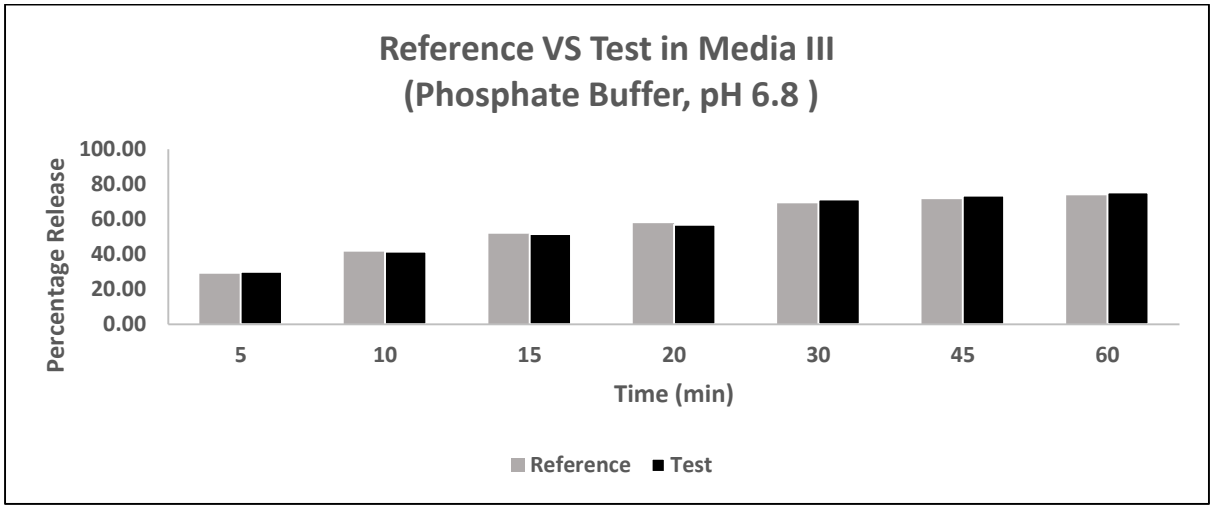
20	69.93	68.37
30	83.50	83.00
45	88.29	87.01
60	92.14	92.63
No. of time points	6	
Similarity Factor	82.86	
Dissimilar Factor	2.02	



The sampling time points up to 45 min are considered in calculation. In acetate medium, the similarity factor and dissimilarity factor are 82.86 and 2.02 respectively.

In Phosphate Buffer, pH 6.8

	% Release	
Sampling Time point (min)	Reference Product (R_t)	Test Product (T_t)
5	28.95	30.09
10	41.46	41.46
15	51.80	51.56
20	57.81	56.93
30	68.99	71.22
45	71.44	73.44
60	73.63	75.30
No. of time points	7.00	
Similarity Factor	88.14	
Disimilar Factor	2.07	



In this case 85% dissolution cannot be reached owing to poor solubility of API. So, all the sampling points are considered in calculation. The similarity factor and dissimilarity factor are 88.14 and 2.07 respectively.

IV. Conclusion:

In an acid medium, more than 85% of drugs were released within 10 min. Similarly, in acetate buffer after 30 min, 85% drugs were released. But in the Phosphate buffer, only 73.63% of the drug was released in the whole dissolution time period. Whatever the release profile, both the innovator and test product show similar response in all three media. In acid media there is no need to calculate similarity factor as it shows more than 85% of drug release within 10 minutes. In acetate and phosphate buffer, 82.86 and 88.14 similarity factor are obtained respectively which fulfills the requirements to test product to be similar with innovator product.

References:

[1]. Tripathi, K.D. (2013) Essentials of Medical Pharmacology. 7th Edition, Jaypee Brothers Medical Publishers (P) Ltd., New Delhi, 816-835
[2]. Zarghi A, Arfaei S. Selective COX-2 Inhibitors: A Review of Their Structure-Activity Relationships. Iran J Pharm Res. 2011 Fall;10(4):655-83. PMID: 24250402; PMCID: PMC3813081.
[3]. Matsumoto AK, Cavanaugh PF Jr. Etoricoxib. Drugs Today (Barc). 2004 May;40(5):395-414. PMID: 15319795
[4]. Samineni R, Chimakurthy J, Konidala S. Emerging Role of Biopharmaceutical Classification and Biopharmaceutical Drug Disposition System in Dosage form Development: A Systematic Review. Turk J Pharm Sci. 2022 Dec 21;19(6):706-713. doi: 10.4274/tjps.galenos.2021.73554. PMID: 36544401; PMCID: PMC9780568.
[5]. Medicine Registration Guidance, 2073
[6]. WHO TRS 1003 Annex 6: Multisource (generic) pharmaceutical products: Guidelines on registration requirements to establish interchangeability.
[7]. Diaz DA, Colgan ST, Langer CS, Bandi NT, Likar MD, Van Alstine L. Dissolution Similarity Requirements: How Similar or Dissimilar Are the Global Regulatory Expectations? AAPS J. 2016 Jan;18(1):15-22. doi: 10.1208/s12248-015-9830-9. Epub 2015 Oct 1. Erratum in: AAPS J. 2016 May;18(3):792. PMID: 26428517; PMCID: PMC4706290.