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Comparison of Dissolution profile for Immediate-Release Dosage form for US and Europe

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Abstract

Any oral medication product control strategy must include the creation of a dissolve method with appropriate specifications. In the creation of drug, dissolution testing is critical IV approach. In some cases, an IV dissolution test can be used instead of an in vivo dissolution test. As a result, regulatory agencies have formally acknowledged in vitro methods to determine the dissolution frequency of API from the solid oral form as a significant factor when manufacturing solid-oral-dosage forms. Dissolution tests have long been acknowledged as critical quality-control tools for ensuring batch-to-batch consistency. Following post-approval changes to pharmaceutical products, dissolution testing is also important in providing quality information of the product.

Keywords: Comparative dissolution profile (CDP), f1 and f2 factor, Office of Generic Drugs (OGD), Vitro/In-Vivo Correlations (IVIVC), European Medicines Agency (EMA), Scale up and post approval change (SUPAC), BCS Based Biowaiver, EMA, Dissolution

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1. Introduction

Comparison dissolution profile could be a graphical illustration in terms of [concentration vs. time] of complete unleash of A.P.I. from a dosage kind dissolved during an appropriate dissolving media. In generic drug company the dissolution testing is an important tool. CDP is wide employed in formulation development, producing method monitoring, and quality control testing. Comparison dissolution is also wont to predict a product' in-vivo conducting. Dissolution testing has been used for the development and approval of generic drugs. Recently, dissolving testing has been increased to different solid generics. In those cases, it's far identified as in vitro testing. Dissolution testing is a substantial position in figuring out the want for bioequivalence profile (BE) research associated with SUPAC. Dissolution and CDP are in-vitro tests that measure the frequency and amount of drug material dissolution from a drug product, often in aqueous solutions under particular conditions. In-vitro drug dissolution studies evaluate the stability of a medicinal product as well as the manufacturing cycle. For BCS I and III API the biowaiver is not requirement.

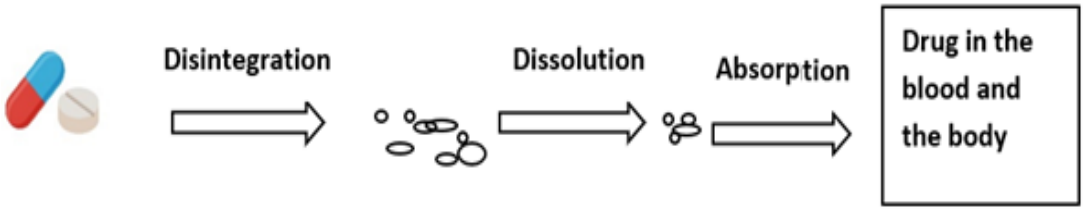

Figure 1. Figure indicates the Tablet/Capsule Disintegration in Body after the administration.

1.1 Introduction to USFDA

The FDA one of the agencies that ensures public safety by enforcing food industry regulations. Drugs for

humans and other animals, cosmetics, radioactive substances, biological and medical gadgets are all applicable to safety and efficacy regulations. Prosecutors in the United States should take the official standards and method introduced in the US Pharmacopeia when working performance to established a dissolution for a replicated (generic) drug that will be selling in the US.

Comparative dissolution testing is required for RLD (reference listed drug) products evaluated by the Division of Bioequivalence, Office of Generic Drugs (OGD), Centre for Drug Evaluation and Research, US-FDA. It is a general chapter on dissolution testing that gives in vitro drug release information, including "batch-to-batch" variability and a substitute for in vivo testing used as In vitro/In Vivo Correlations (IVIVC) and USP General Chapter 711, the dissolution test is in accordance with European and Japanese standards.

There are available sorts of approaches to setting generic product dissolution specifications.

- If a USP Drug Product Dissolution Test is available, it should be used.
- If USP Drug product Dissolution test is available, it should not be used. (1)

1.2 Introduction to EMA

The EMA is a decentralised organisation, which take charge of scientific analysis, oversight, and safety monitoring of medicines throughout Europe. The EMA governed the management board. Employees of the EMA carry out activities, which has been directed by the EMA's chief director. The EMA may be a networking organisation with thousands of consultants from all across Europe participating in its events. The European Medicines Agency (EMA) reviews applications from companies seeking to sell generic drug in the European Union (EU). European Pharmacopoeia 8.0 and 5.17.1. Dissolution test recommendations give information on dissolution testing, recommendations for dissolution medium, and expressed of dissolution specifications for the oral dosage form. (2,3)

Table 1. IR Dissolution Specification (4)

SR NO.	US	EUROPE
1	Considering bio batch results (Reference vs test product) the dissolution limit for release & shelf-life specification is to be identify as per guidance of immediate release dosage form.	Considering bio batch results (Reference vs test product) the dissolution limit for release & shelf-life specification is to be identify as per EMA reflection paper.
2	For US immediate release dosage form dissolution at least should be kept Q=80% of drug substance dissolved in 45 minute.	For EUROPE immediate release dosage form dissolution at least should be kept Q=75% of drug substance dissolved in 45 minute.

2. Regulatory Landscape

While the EU and the US have traditionally has been at the leading of dissolution advice, current trends show that regulatory bodies throughout the globe are increasingly requiring specific dissolution similarity standards.

Many international regulatory bodies propose using the f2 similarity factor to indicate dissolution similarity. This method is simple to implement, the f2 value is straight forward to compute and calculation is done when the f2 value is more than 50. For medicine's Biopharmaceutics Classification System (BCS) classification and therapeutic index should also be considered. (5)

Table 2. Similarity and dissimilarity of F1 and F2 factor

SR No.	F1 factor	F2 factor
1	Called difference factor	Called similarity factor
2	When F1 between o and 15, Two dissolution profile should be regarded comparable and bioequivalent	When F2 between 50 and 100, Two dissolution profile should be regarded comparable and bioequivalent
3	f1 calculated the percentage (%) difference between the two curves at each time point and is a measurement of the relative error between the two curves.	The percentage (percent) dissolution similarity between the two curves is measured by f2.
4	Use to compare two dissolution profile where one of them as reference standard product.	When more than three or four dissolution time points are available, this factor is more preferred.

3. What is comparative dissolution method?

Most regulatory governments suggest that the f2 component be undertaken for a predetermined reference (perchance) and test (post-change) drug product lots to efficiently bridge components and production process-associated adjustments within side the preapproval or post-approval space. Three production batches in Japan and Korea are tested, and the batch with the medium dissolution rate is selected as the reference batch; Similarly, three post-switch production lots are tested and the lot with the medium dissolution rate is selected as the test lot. The dissolution profiles of the reference and test products are generated using a validated disintegration procedure that includes the media listed in the regulatory submission plus two additional media including such:

1. 0.1 N HCl
2. pH 4.5 acetate buffer
3. pH 6.8 phosphate buffer

The evaluation of the product should be carried out in three media to access dissolution performance through relevant physiological pH range. The specific consideration to media selection should be carried out in case where multiple time points and multiple media testing is necessary. For example, pH range should be justified in case of use of water as dissolution medium and dissolution media. (6)

4. BCS Based Biowaiver

- Used to eliminate in vivo bioequivalence
- Only applicable for IR dosage form (Class I & Class III)
- Drug substance in test and reference are known then and then the Biowaiver can applicable (7,8)

Table 3. CDP difference between USFDA and Europe (2,4,9)

SR.NO	REQUIREMENT	USA	EUROPE
1	Apparatus	Paddle or basket	Paddle or basket
2	Volume of dissolution medium (ml)	500,900,1000	900
3	Temperature of dissolution medium	37± 0.5 Celsius	37 ± 1 Celsius
4	Agitation	➢ Basket (USP apparatus 1) -100 rpm ➢ Paddle (USP apparatus 2) – 50 rpm	➢ Basket -100 rpm ➢ Paddle – 50 rpm
5	Suggested pH media for CDP	➢ As per OGD media ➢ (Product specific dissolution method) ➢ If product is USP pharmacopeial than Monograph method should adopted.	➢ pH 1.2 buffer or 0.1 N HCL pH 4.5 acetate buffer ➢ pH 6.8 phosphate buffer
6	Numbers of tablets (for CDP)	12	12
7	Surfactant/organic solvent acceptable	NO	NO
8	BCS CLASS FOR IR	➢ BCS class I API biowaiver can do. BCS class II, III, & IV Bioequivalence study and QC release media is required	➢ BCS class I & class III API biowaiver can do. ➢ BCS class II & IV bioequivalence study and CDP (Test vs RLD)
9	Multimedia test	➢ QC release media	➢ Not acceptable for BCS class II & IV.
10	CDP report	➢ YES	➢ YES

5. Conclusion

Comparative dissolution profile accounts for drug product dissolution, solubility, and API permeability. For rapidly dissolving IR tables containing class 1 API, BCS-based biowaiver can be obtained by the dissolution profile or original dosage form. By comparing the regulatory requirements for dissolution Method of US and Europe a brief understanding of both the countries can be known. The different regulatory agencies followed the guidance documents should be undertake when applying the similarity factor approach to comparing in vitro dissolution profile & f2 is a basic tool for dissolution profile similarity assessment.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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