Drug Dissolution Testing For Global Bioequivalence Requirements

By

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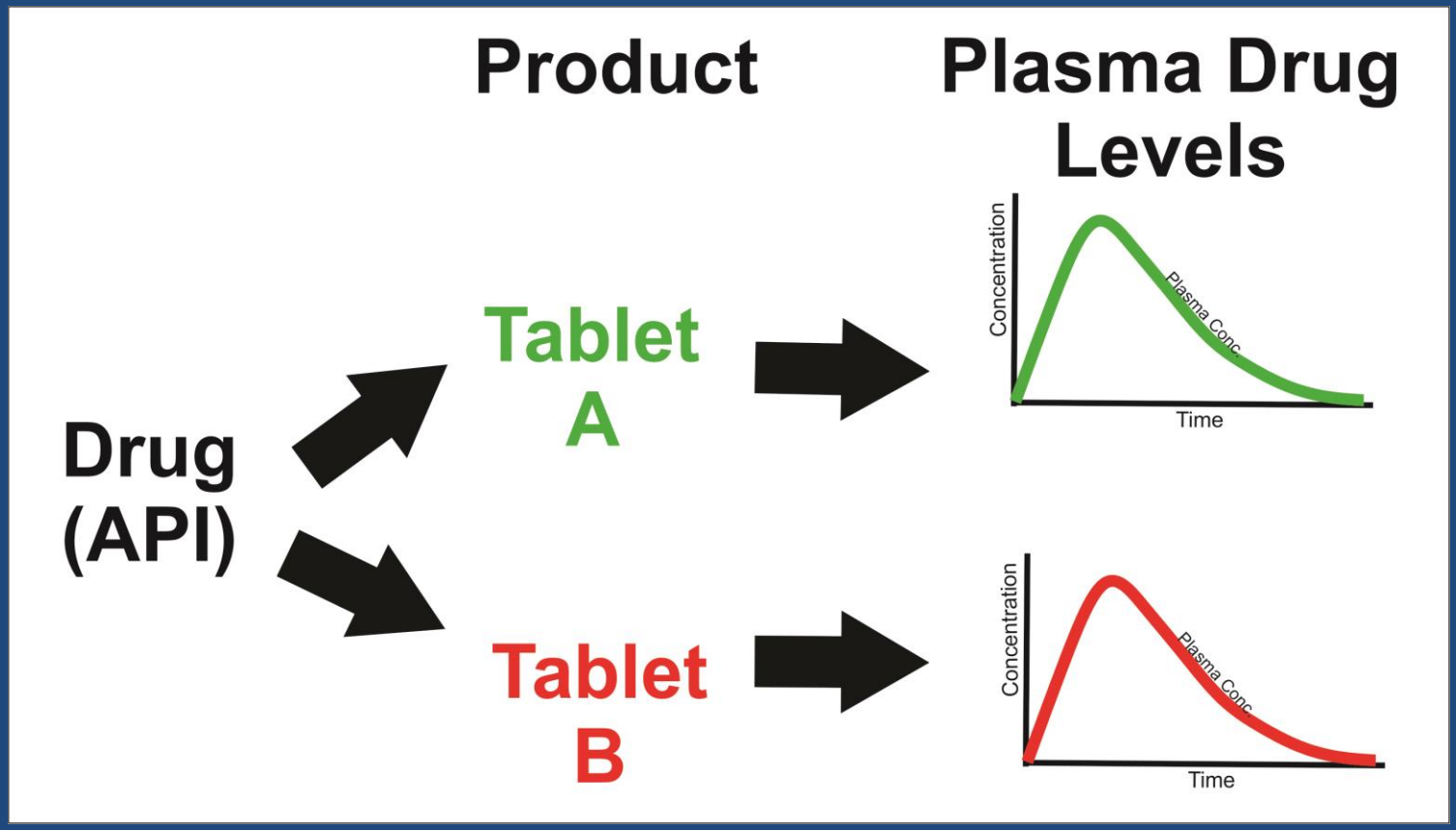
What is bioequivalence?

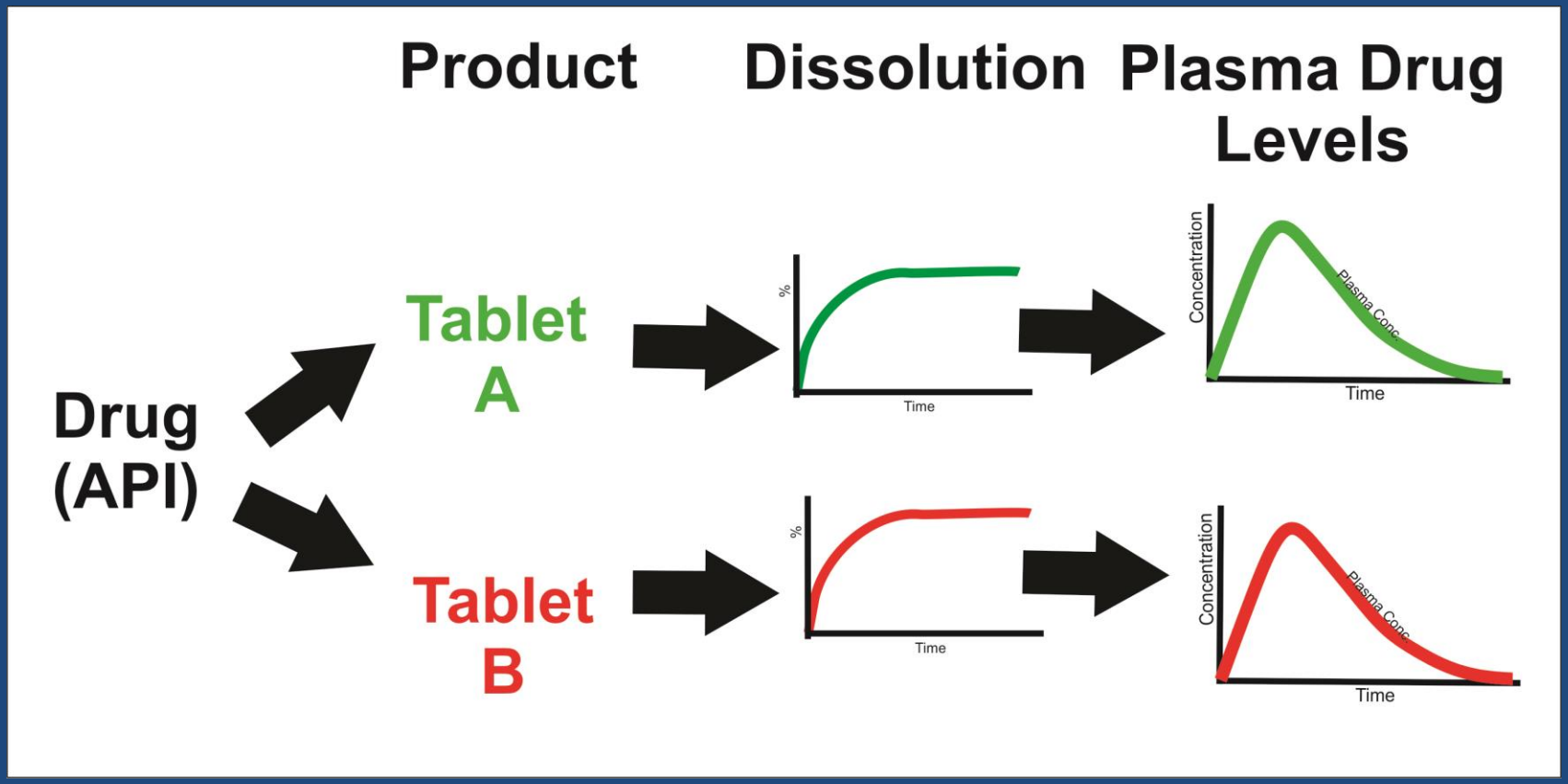
Bioequivalence means the absence of a significant difference in the rate and extent to which the active ingredient (…..) becomes available at the site of drug action when administered at the same molar dose under similar conditions in an appropriately designed study. (FDA definition, *Link*)

What is bioequivalence? - 2



Two or more products provide same plasma drug levels/profiles

What is bioequivalence? - 3



In reality, products provide same drug dissolution/release rate

Bio-equivalence and quality of products

Thus, drug dissolution or release characteristic becomes quality attribute/metric of a *product*.

This is what we measure, or need to measure, if we like to establish quality of a drug product.

Quality of products

Quality of a drug product is its ability to release drug in vivo or in humans in an expected and consistent manner.

A quality product?

Is this a quality product?

Yes, ***if*** it (product) releases drug as expected and consistently.

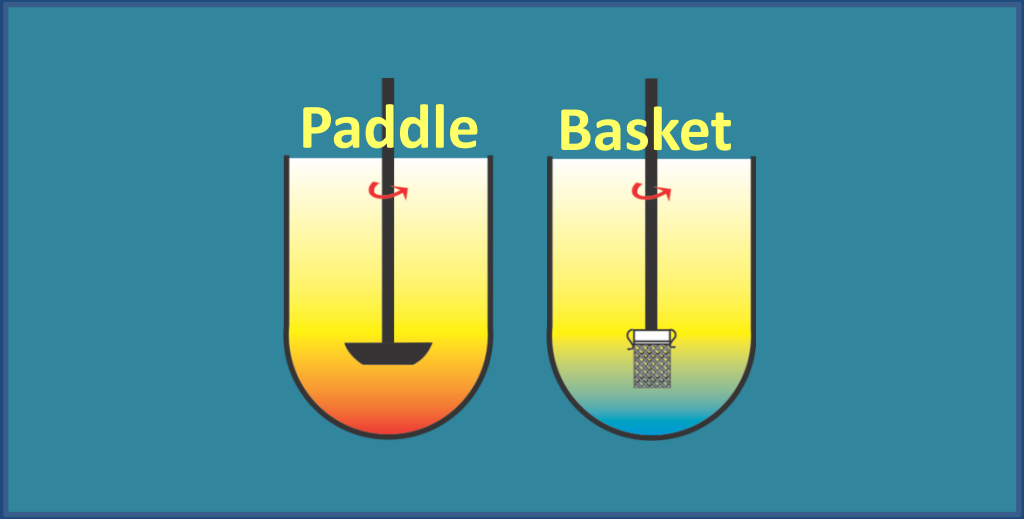
Measuring Bio-equivalence

- *In vivo:* it is measured with plasma drug conc.-time profiles.

- *In vitro*: it is measured using a test known as drug dissolution test.

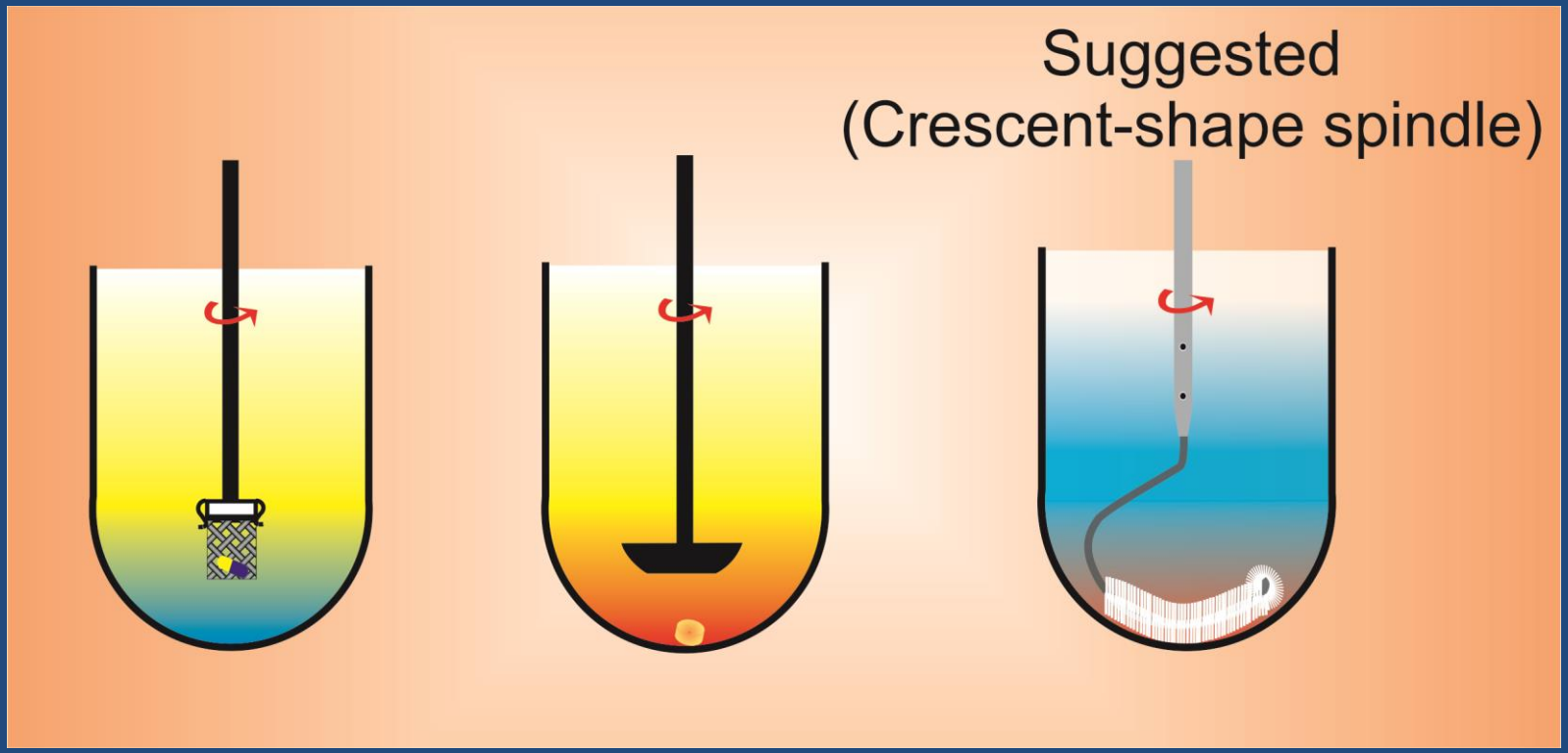
Dissolution testers

Specialized beakers and stirrers known as -



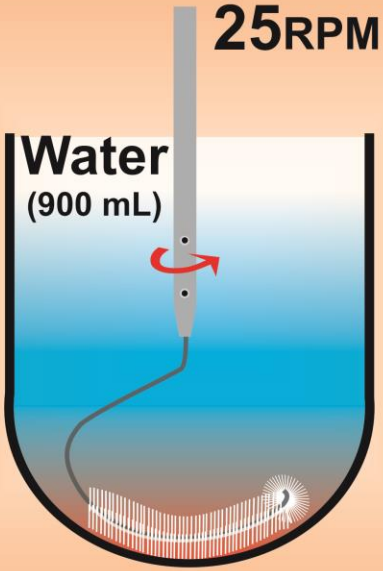
With rotation speed between 50 to 100 rpm – as per pharmacopeias e.g. USP

Dissolution testers - 2



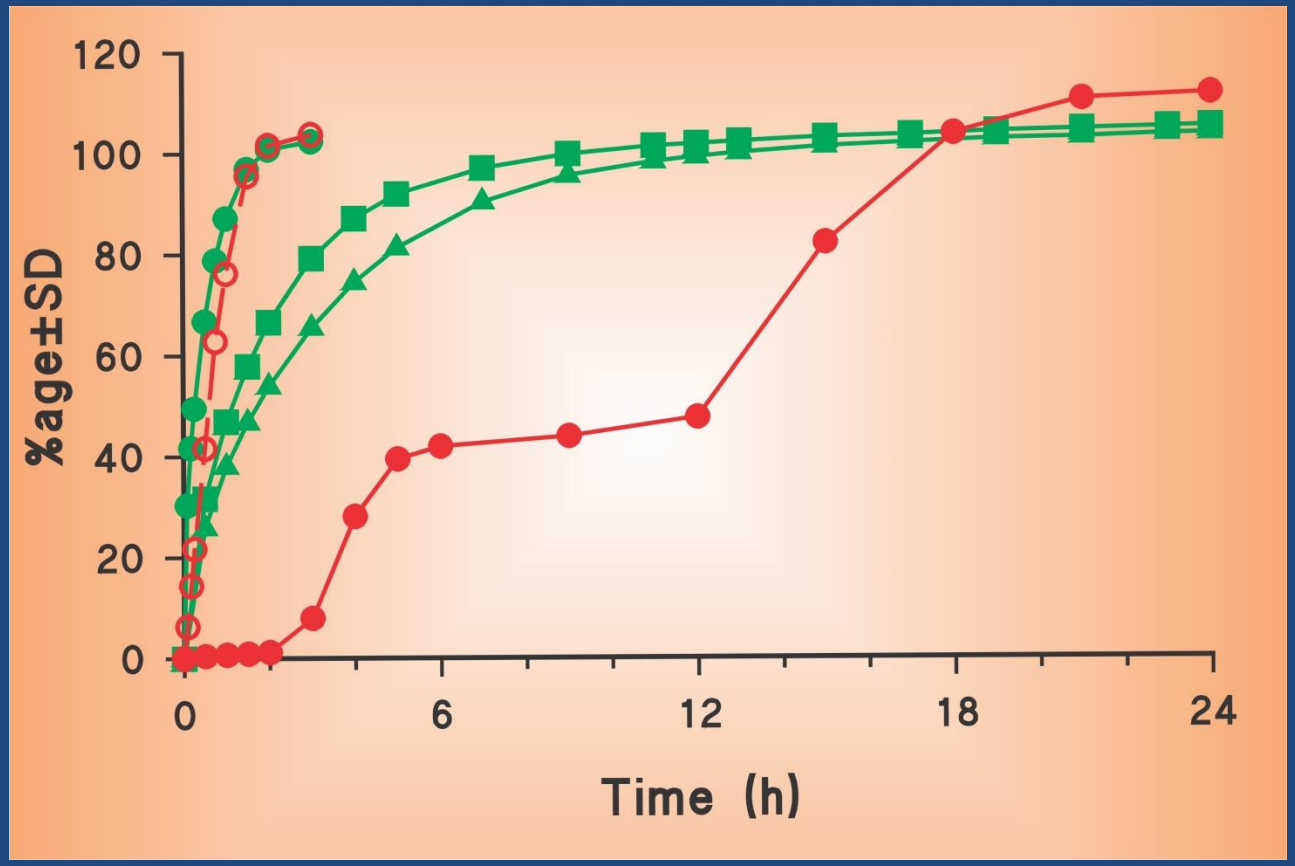
Avoids stagnation and cone formation, thus provides improved stirring and mixing.

Dissolution testers - 3

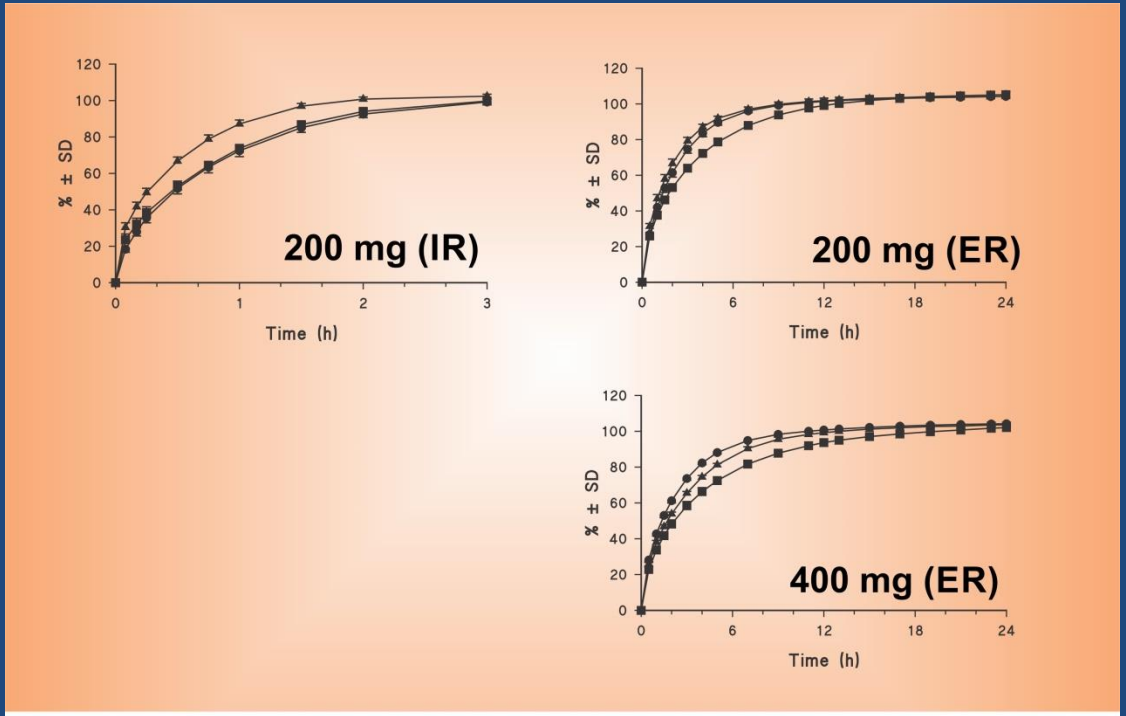


Dissolution testing using crescent-shape spindle

Dissolution testing – Diltiazem products



Dissolution testing – Carbamazepine products



Dissolution characteristics of multi-vendor carbamazepine products using Crescent-shaped spindle (identical experimental conditions)

Summary and conclusions - 1

- **Bioequivalence is the assessment of similarity of plasma drug conc.-time profiles which are indirectly a reflection of in vivo dissolution characteristics of the products.**
- **The in vivo dissolution characteristics represent quality attribute of a product, in particular tablet and capsule.**
- **For manufacturing (pre-, post- or during) dissolution characteristics are assessed using in vitro dissolution methods.**
- **The commonly suggested dissolution testers are neither validated or qualified for the purpose, and are not able to provide useful in vivo dissolution characteristics.**

Summary and conclusions - 2

- **Thus, unfortunately at present, one cannot established quality of the products at the manufacturing stage.**
- **A modified stirrer, known as Crescent-shape spindle, has been suggested to address the current deficiencies of the drug dissolution testing.**
- **The suggestion provides a simple and universal dissolution testing approach leading to improved and physiological relevant testing.**

Thank you!