Choice of Excipients and their impact on Dissolution

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Agenda

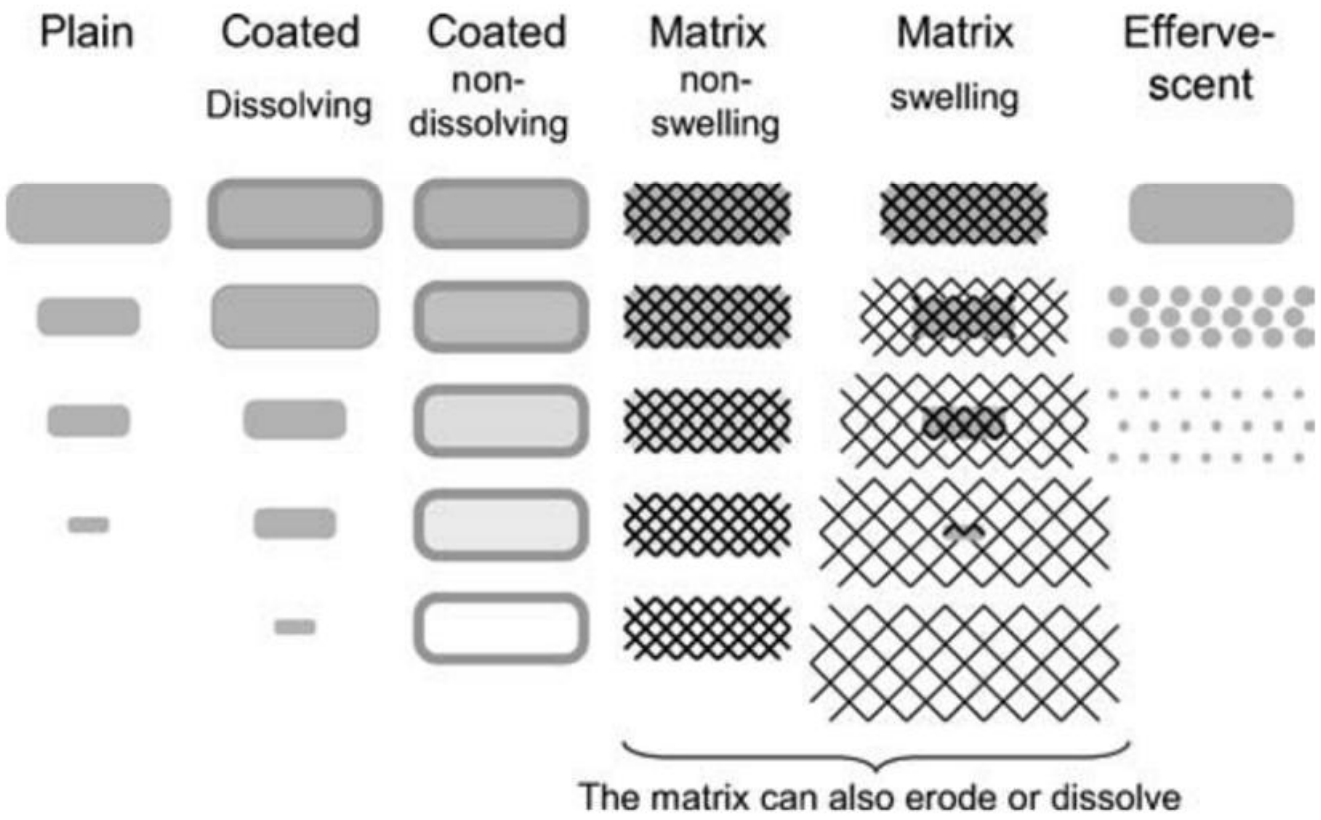
- Definition
- Classification
- Dissolution basics
- Case studies

Definition

Any substance, other than the active drug or product, that have been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing of the drug delivery system during its manufacture, protect, support or enhance stability, bioavailability, or patient acceptability, assist in product identification or enhance any other attribute of the overall safety and effectiveness of the drug delivery system during storage or use.

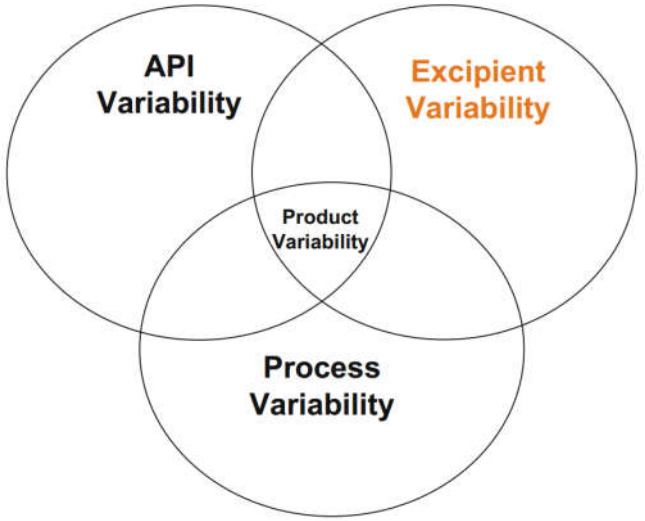
Classification

- Inert
- Functional



Understanding Excipients

- QbD
- Excipients enable API's
- Major source of variability
- Impacts CQA
- Patient safety
- Speed to market

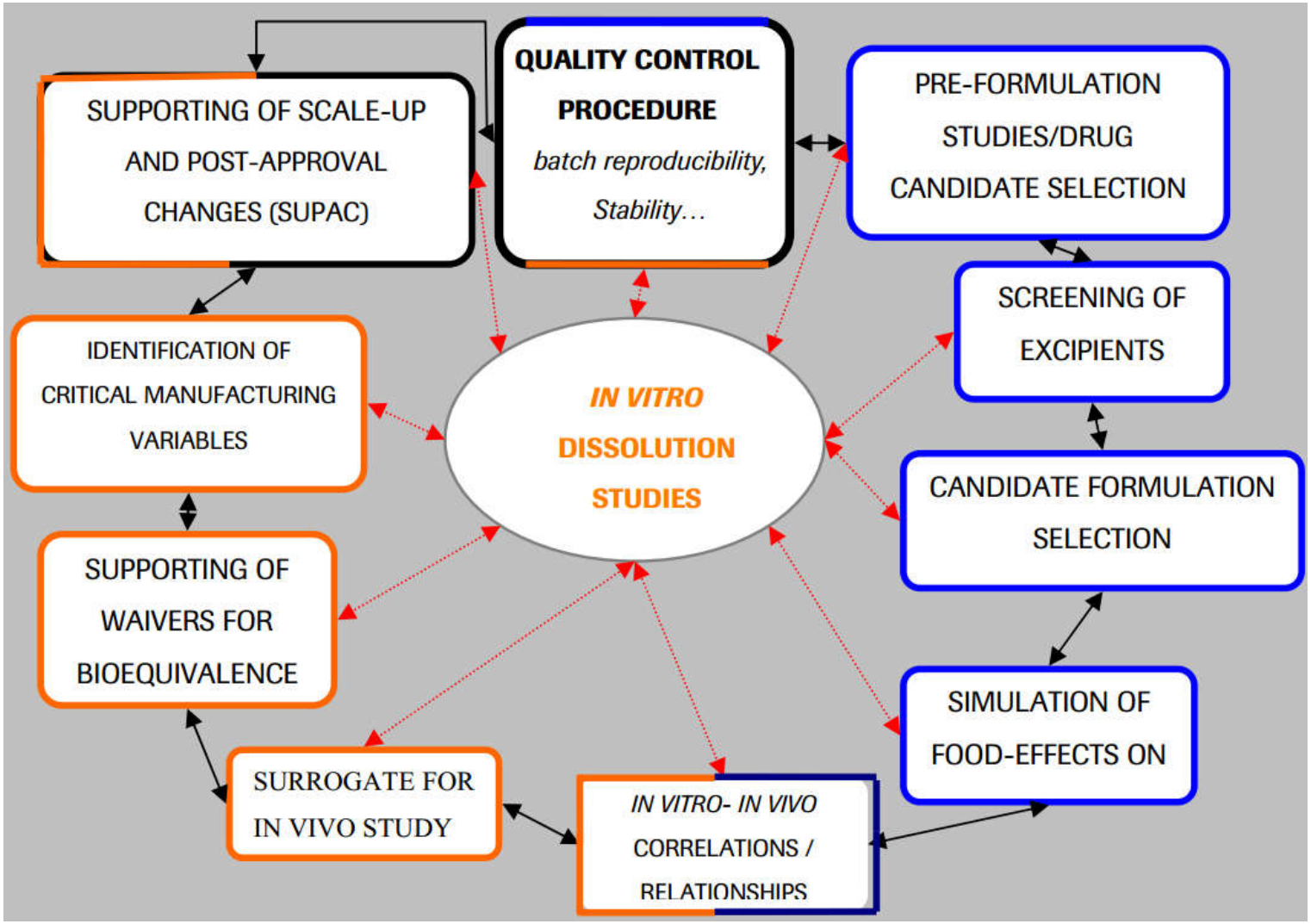


Understanding variability & tolerating it = Robustness

$$\sigma^2_{Product} = \sigma^2_{API} + \sigma^2_{Excipients} + \sigma^2_{Process} + \sigma^2_{Interactions}$$

Ref: C. Moreton

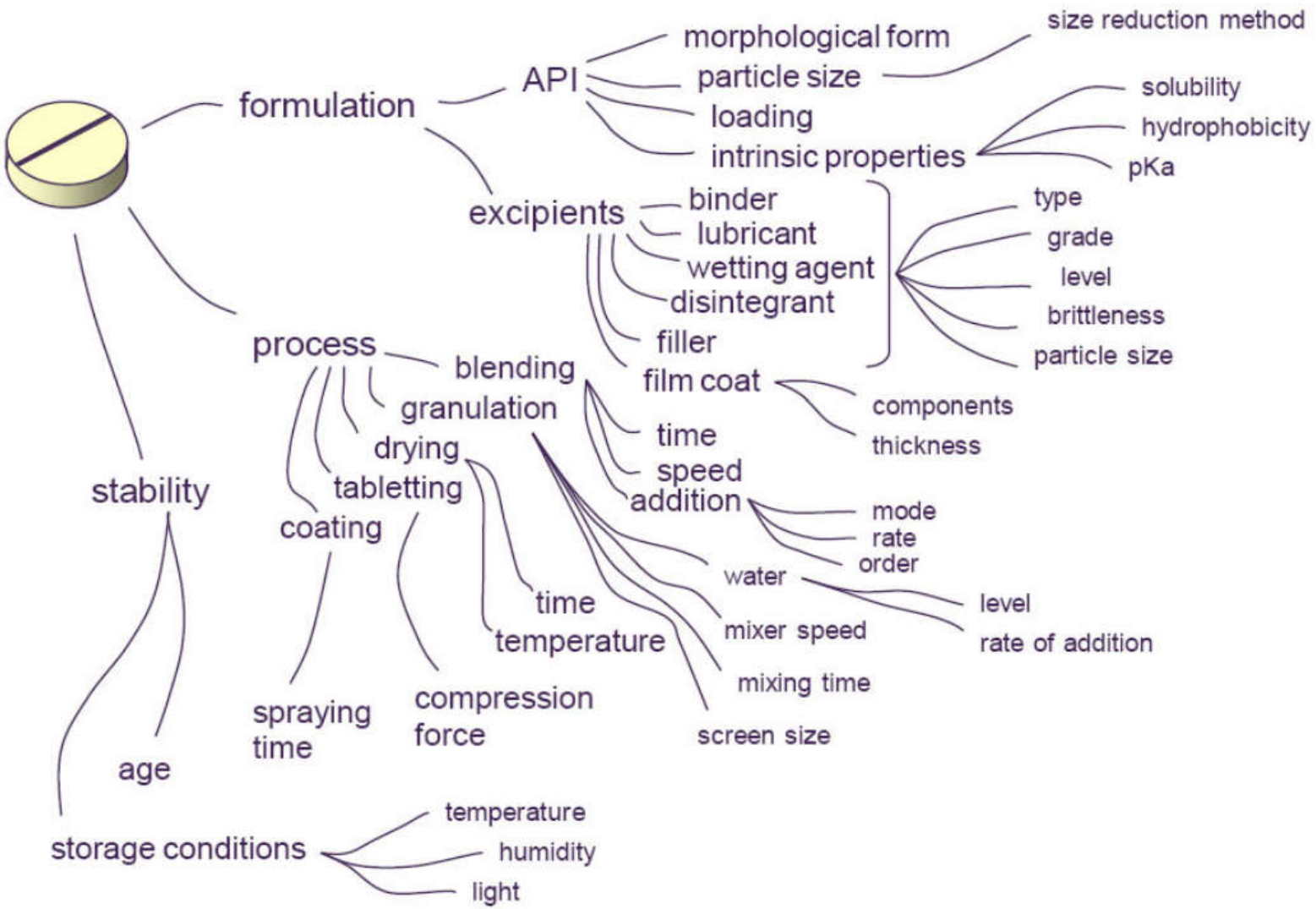
Central Role of Dissolution



Ref: Emmanuel Scheubel

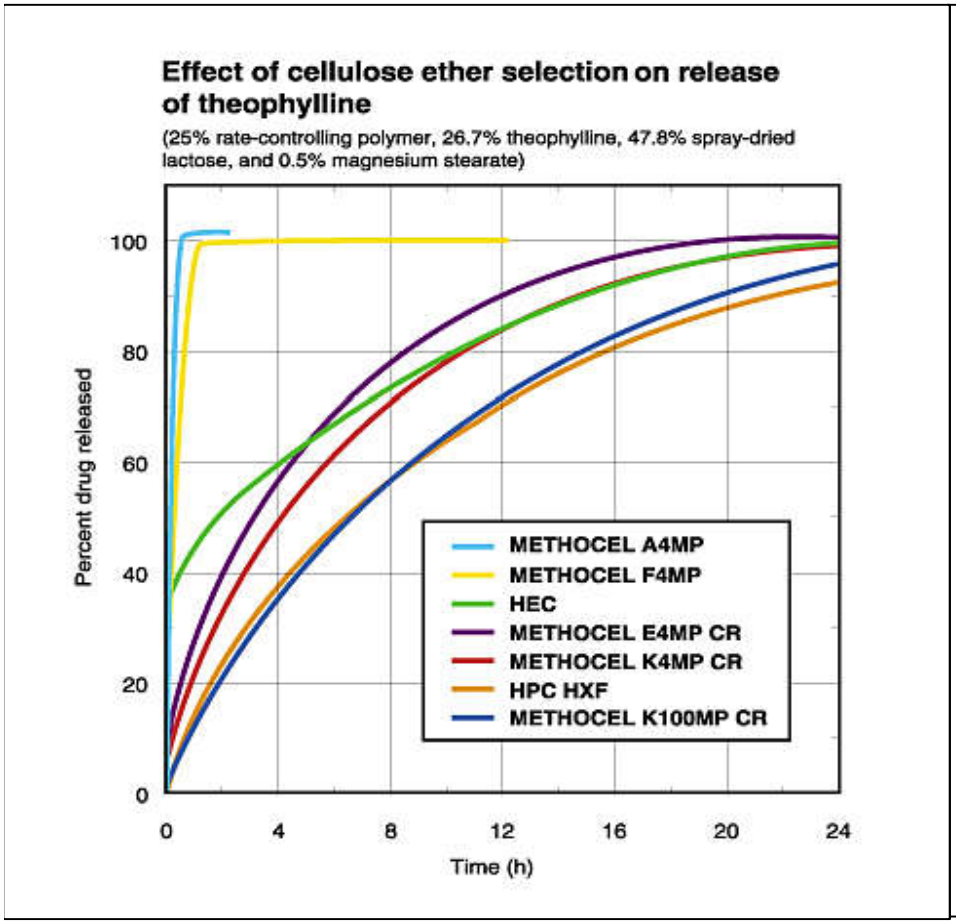
Early phase of development — Late phase — Market

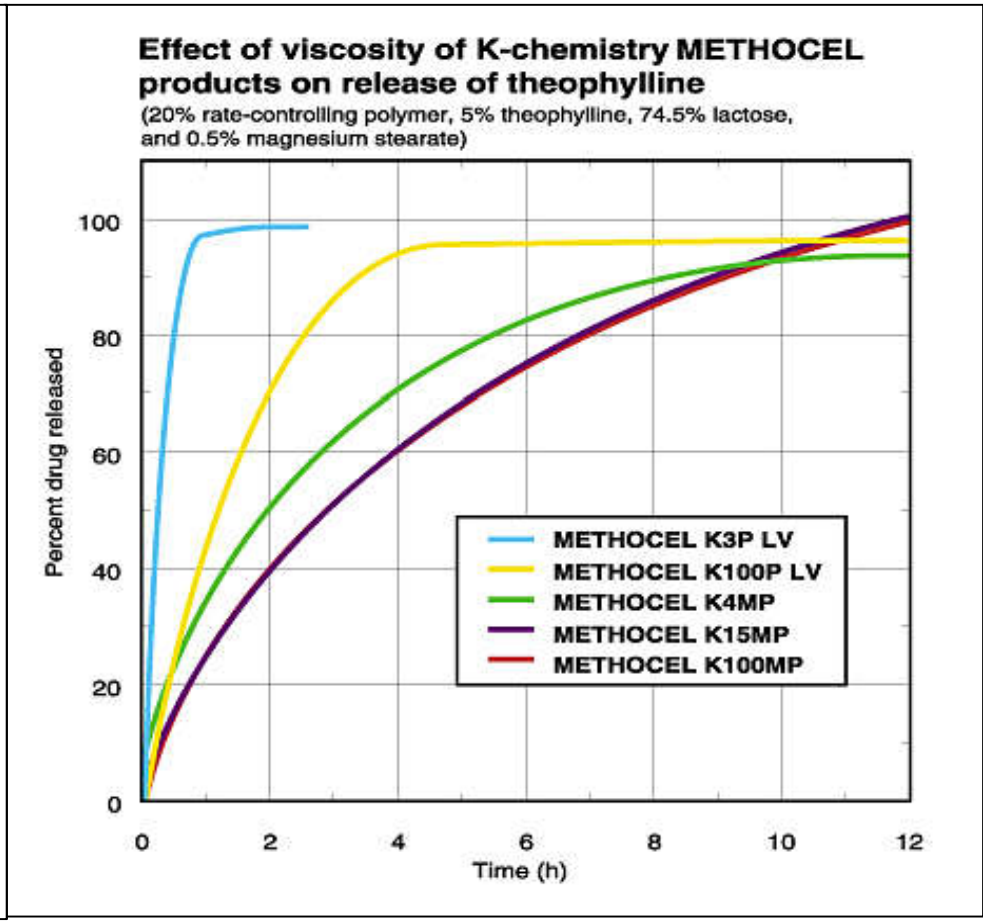
Factors affecting in-vitro dissolution



Dr Donald Murphy, Astra Zeneca UK, IRR Conference, May 07, Budapest

Hydrophilic Matrix

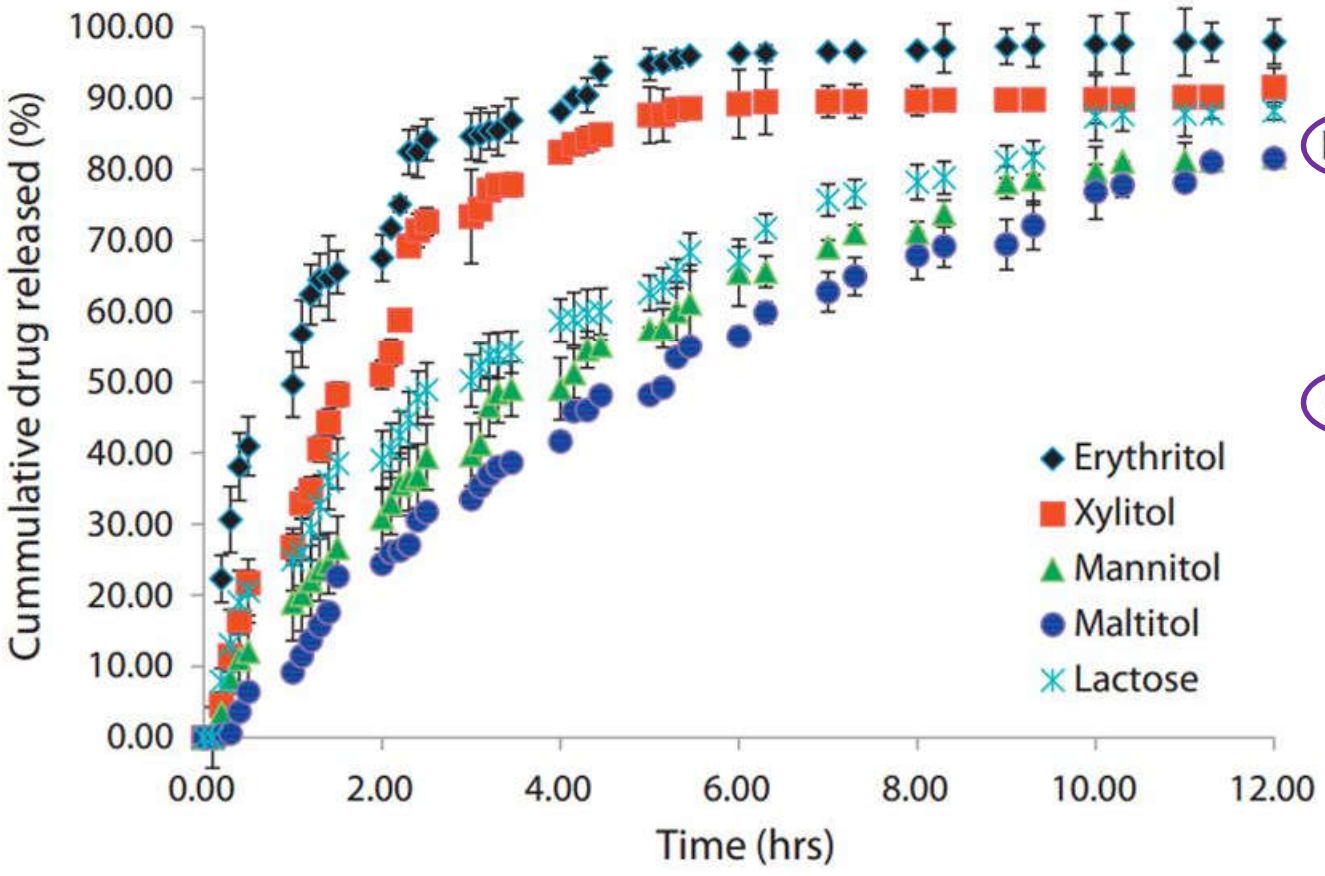


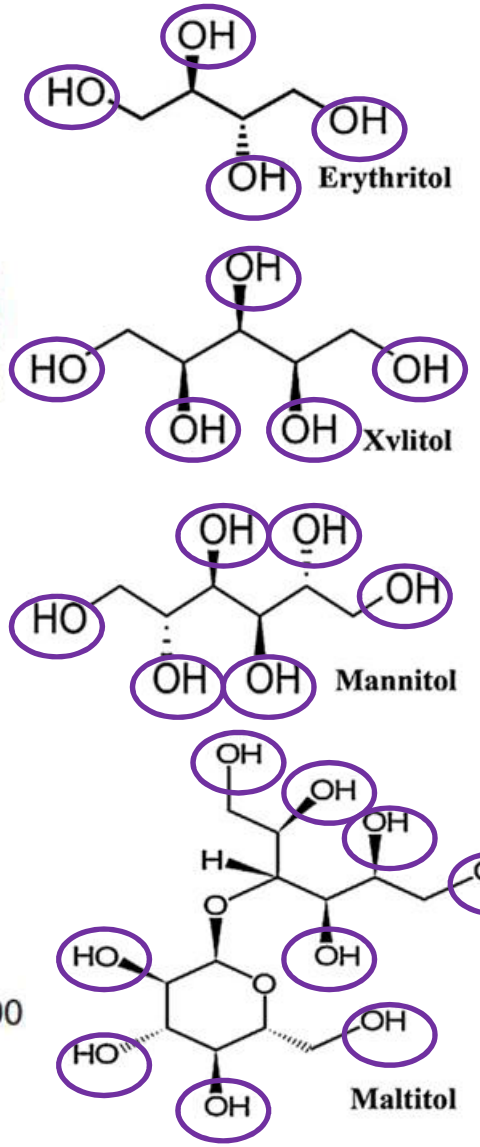


Dow Methocel Handbook

Release Modulation: Diluents

Colloids and Surfaces B: Biointerfaces 111 (2013) 24–29





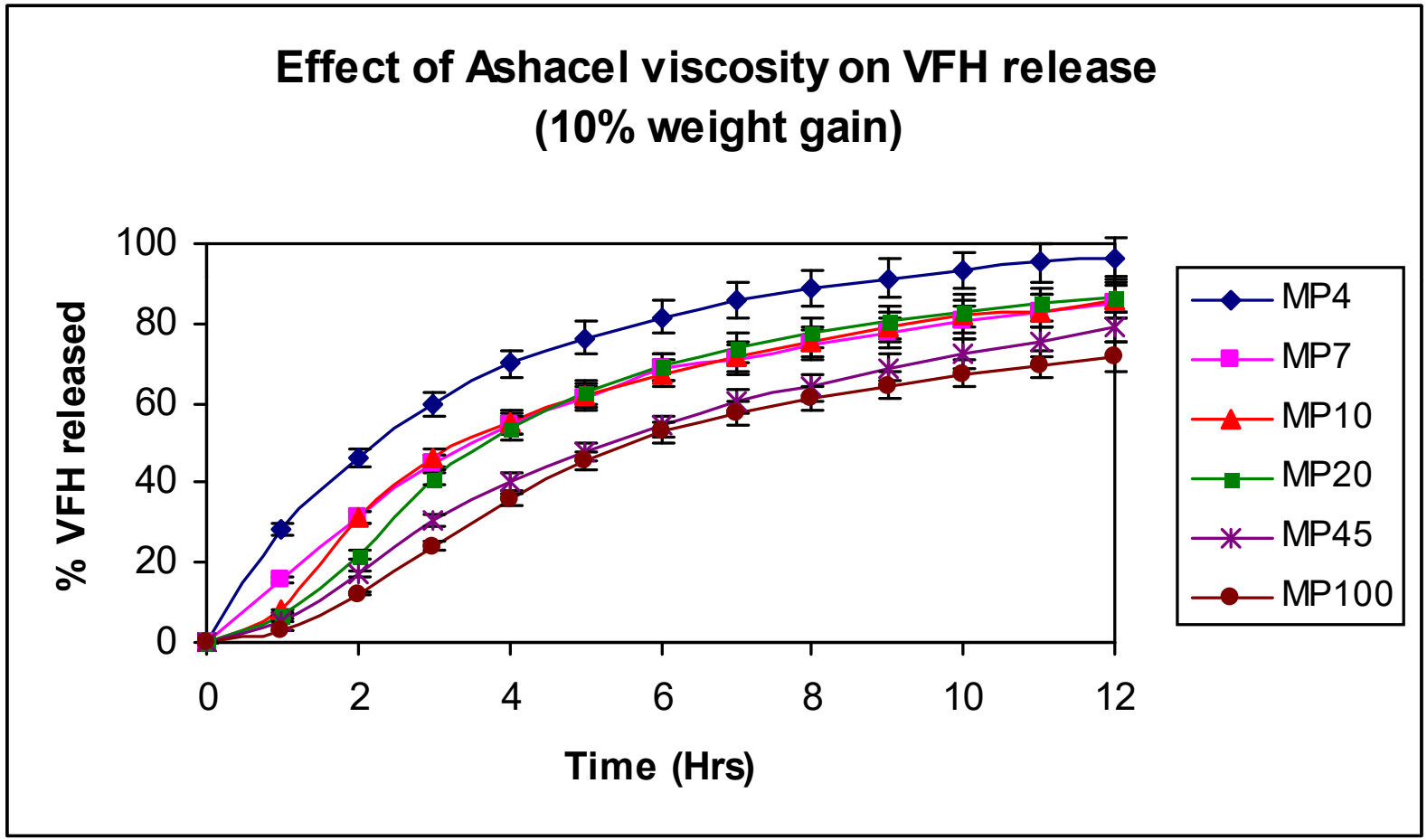
Effect of the type of polyol on theophylline release from polyol-HPMC matrices.

Effect of Ethyl cellulose viscosity

Venlafaxine HCl dissolution

Dissolution conditions:

Medium: 900 ml of 0.1N HCl; Apparatus: Paddle; Speed: 50rpm

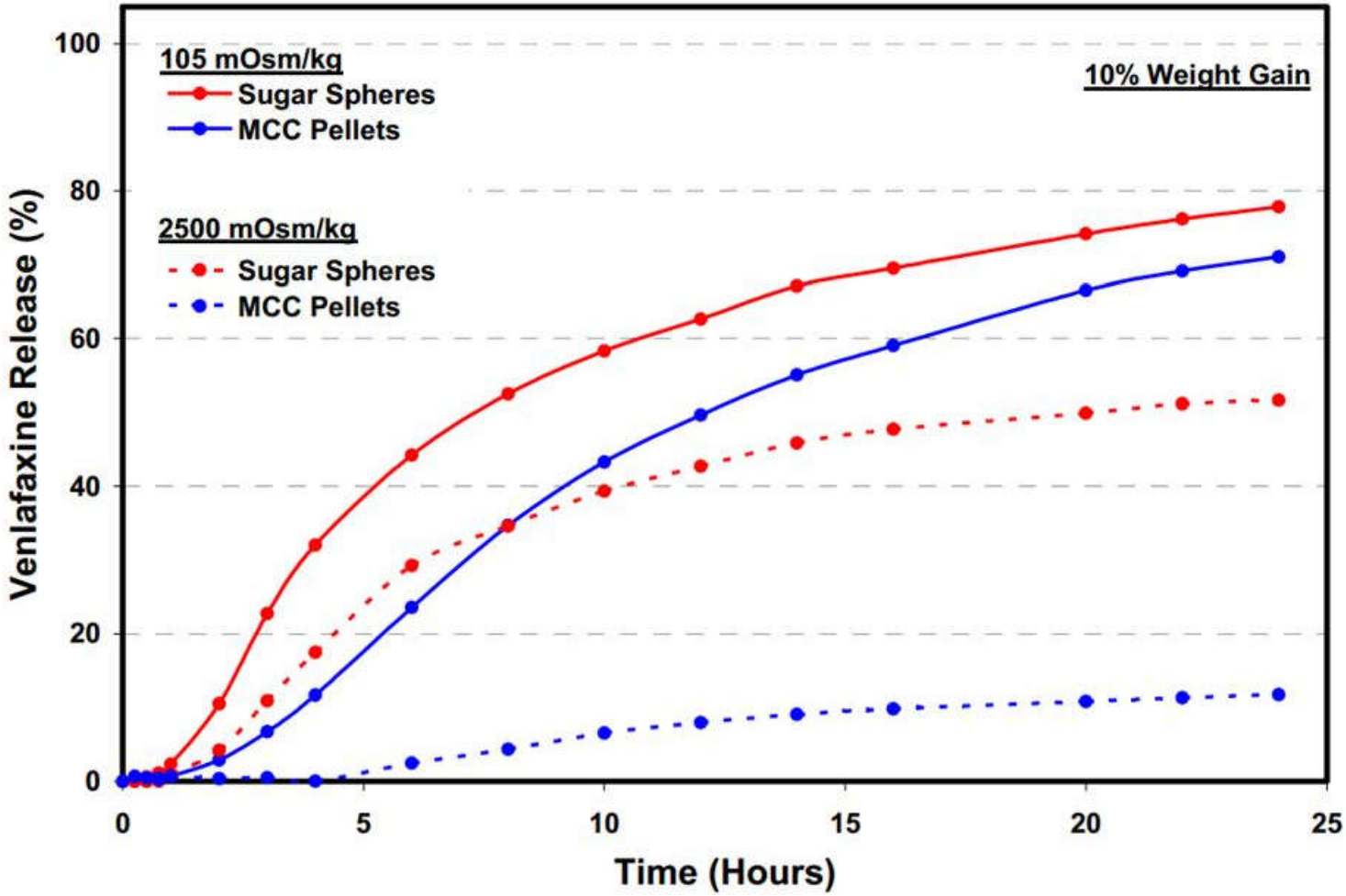


Effect of Core Pellet Composition

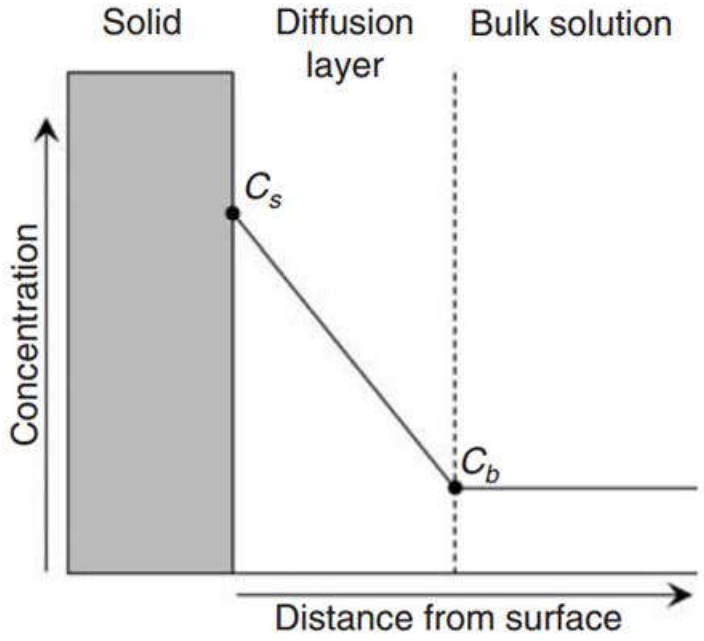
Venlafaxine HCl dissolution

Dissolution conditions:

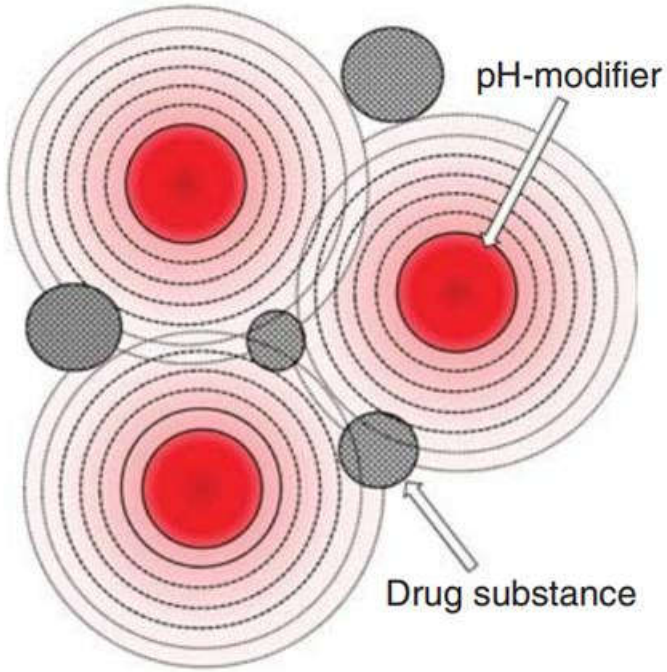
Medium: 900 ml of 0.1N HCl; Apparatus: Paddle; Speed: 50rpm



Controlling micro-enviornmental pH

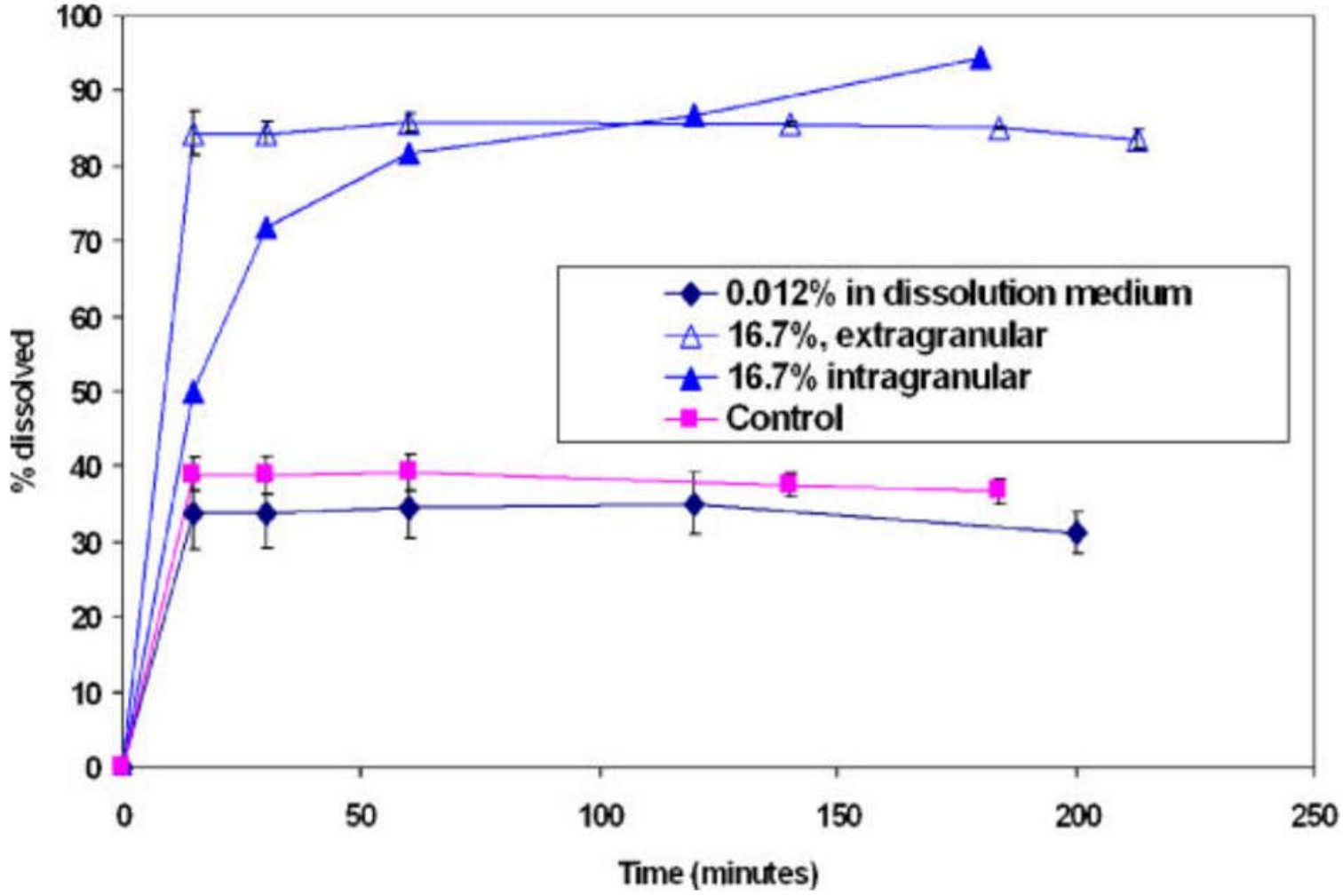


(A) Diffusion layer model of drug dissolution from solid. C_s, the saturation solubility of the drug at the solid interface; and C_b, the concentration of the drug in bulk medium.



(B) The image of creating a favorable microenvironmental pH for drug dissolving in the microenvironmental pH-modification approach.

Controlling micro-enviornmental pH



Effect of tartaric acid on the dissolution profile of Razaxaban HCl tablets in acetate buffer, pH 5.5

Badawy SIF, Gray D, Zhao F, Sun D, Schuster A, Hussain MA. 2006. Pharm Res 23: 989–996.

Summary

- Excipients are not inert
- Excipients dictate the drug release
- Right selection of excipients is essential for successful formulation development.
- Understanding excipients is key to bio-behaviour.

Thank you