

„The Practice of Dissolution Testing in Herbal Medicinal Products“



The impact of dosage forms

Anna Rita Bilia

Department of Pharmaceutical Sciences
University of Florence
E-mail: ar.bilia@unifi.it

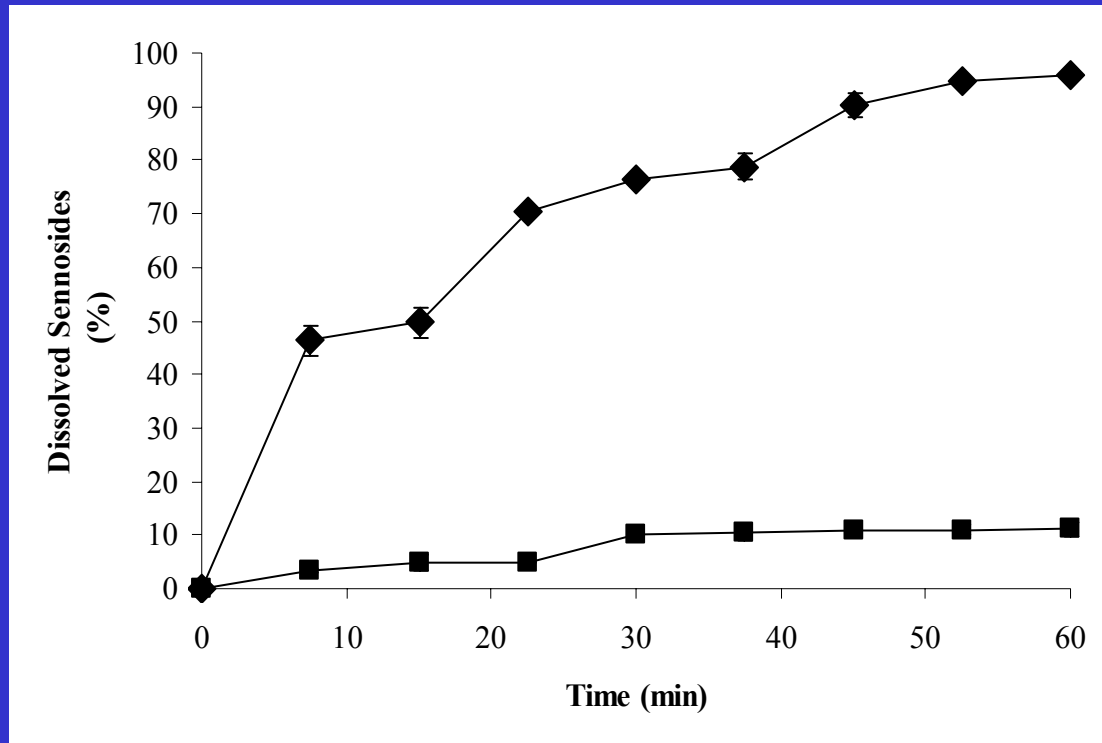
GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“



Dissolution behaviours of Senna preparations

◆ freeze-dried extract

■ powdered HD



“Herbal Drugs vs Herbal Drug Preparations”

GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies”



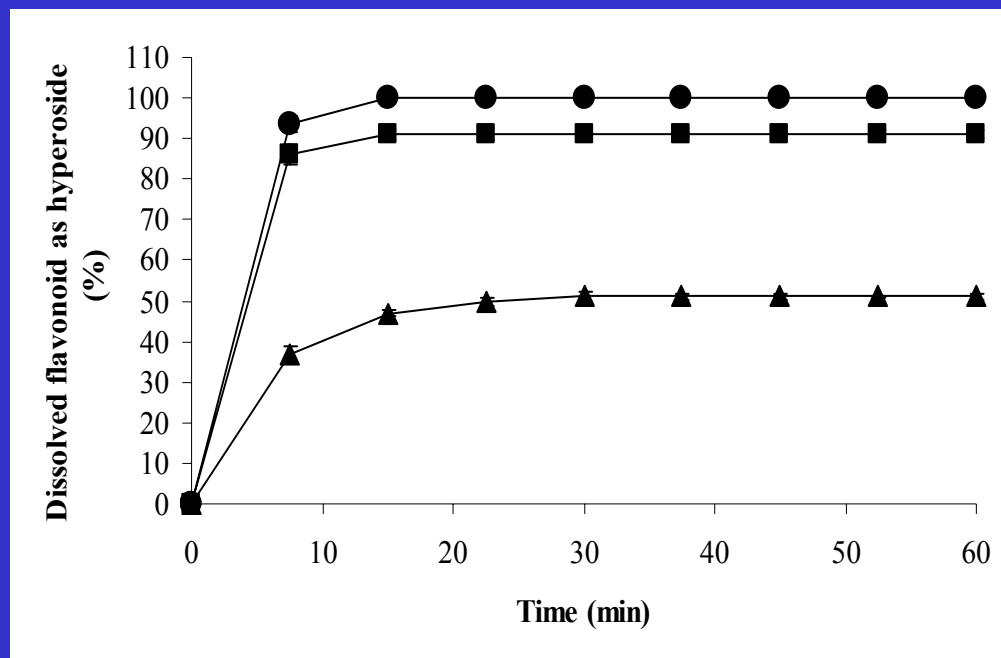
Medium : Distilled water , $37^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,

Rotation speed: 50 rev/min

Taglioli, Bilia, et al. (2001) *Pharmazie*, 56 (11), 868-70

Dissolution behaviours of Passiflora preparations

- ▲ powdered HD
- Passiflo2
- freeze-dried extract



“Herbal Drugs vs Herbal Drug Preparations”

GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies”



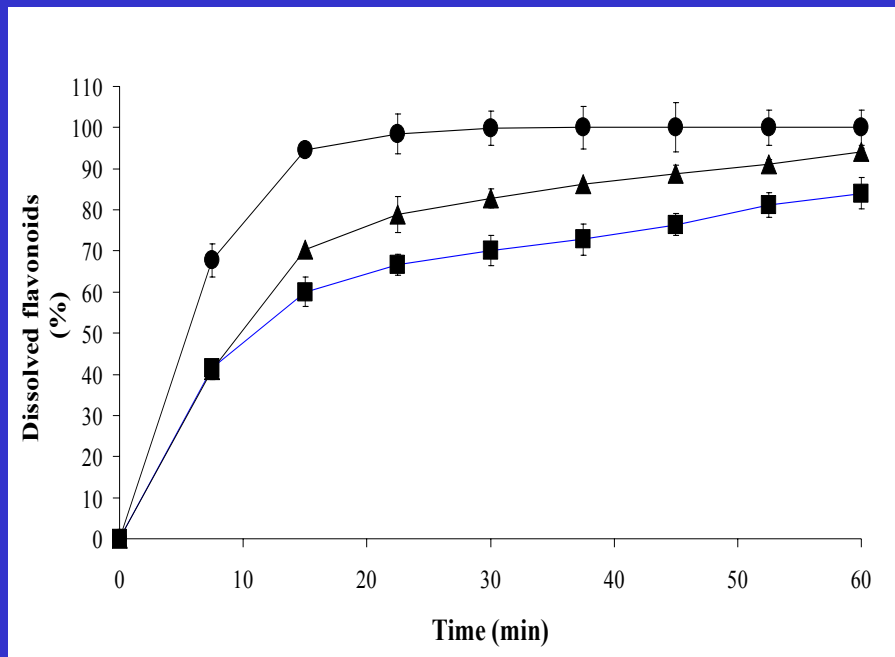
Medium : Distilled water , $37^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,

Rotation speed: 50 rev/min

Taglioli, Bilia, et al. (2001) Pharmazie, 56 (11), 868-70

Dissolution behaviours of Ginkgo preparations

- ▲ freeze-dried extract
- granulate extract
- powdered HD



“Herbal Drugs vs Herbal Drug Preparations”

Medium : Distilled water , $37^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,

Rotation speed: 50 rev/min

GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies”



Taglioli, Bilia, et al. (2001) Pharmazie, 56 (11), 868-70

"Herbal Drugs vs Herbal Drug Preparations"



➤ Differences in dissolution profiles could result from solubility, surface area, particle size, hydrodynamic or diffusivity differences.



➤ Passiflora preparations:

"Passiflo2 and freeze-dried extract"

>> powdered HD



➤ Excipients in the formulation could influence solubility and wettability of the constituents and perhaps exert a minor effect on their diffusivity

➤ ...Solubility and rapid dissolution of an API is of superior importance than its permeability...

and...solubility and dissolution behaviour can be pharmaceutically controlled

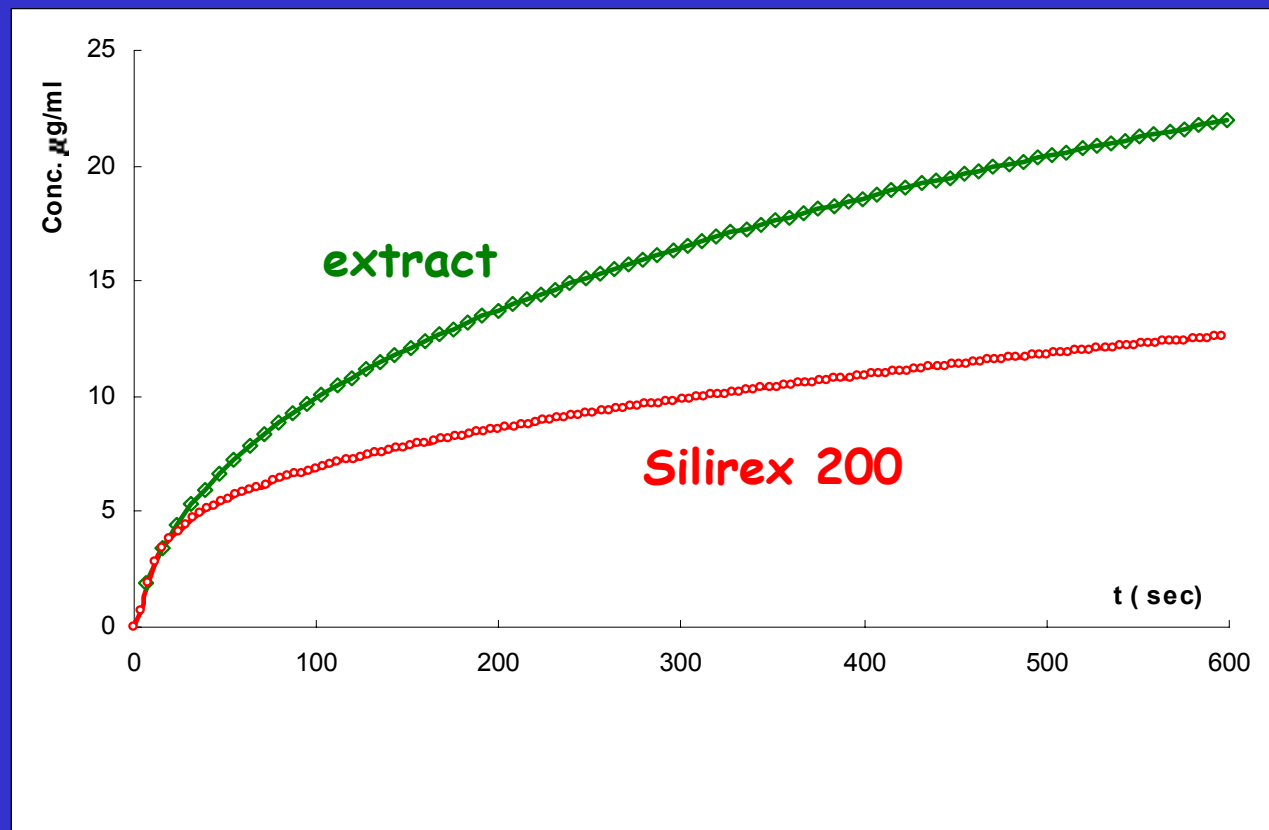
NfG on the investigation of bioavailability and bioequivalence
(intended mainly for chemically defined products, CPMP/EWP/QWP/1401/98)

Dissolution testing in the presence of polymers



GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“





Medium : Distilled water , $37^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,

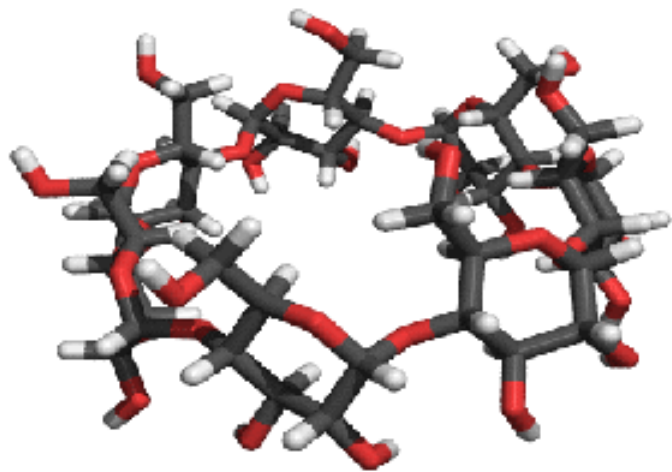
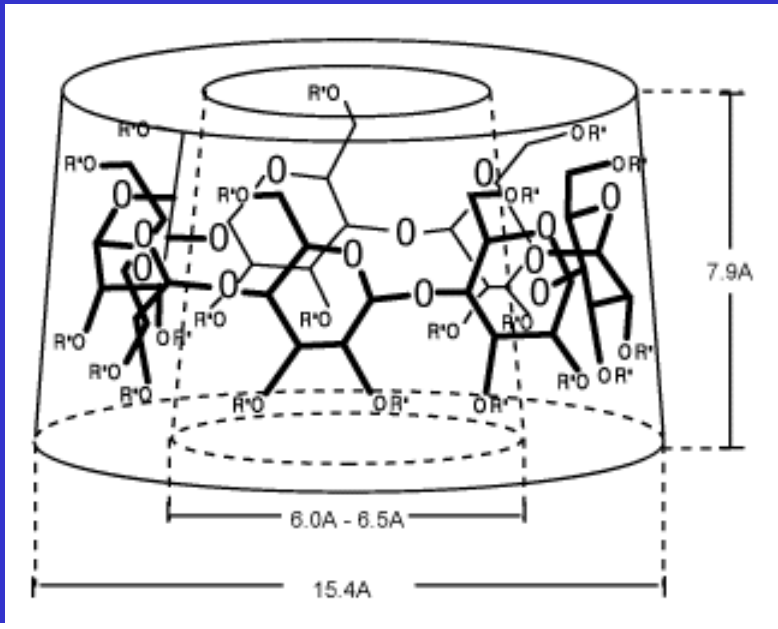
Rotation speed: 100 rev/min

40 mg silybin A+B / 600 ml, $\lambda = 287 \text{ nm}$

GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“



Beta-cyclodextrin

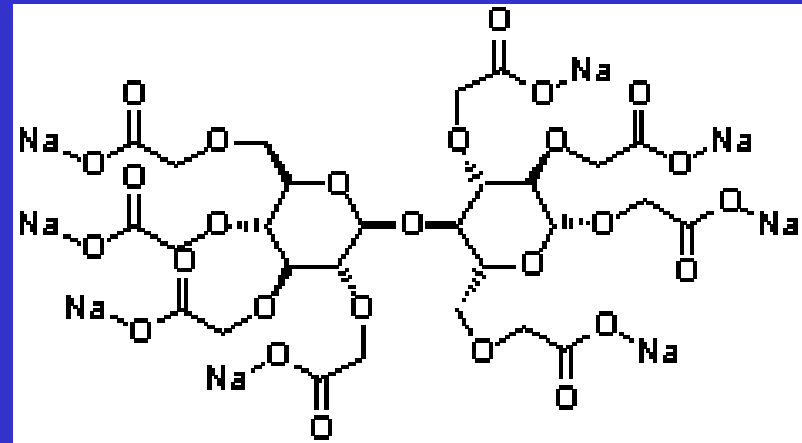


GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“



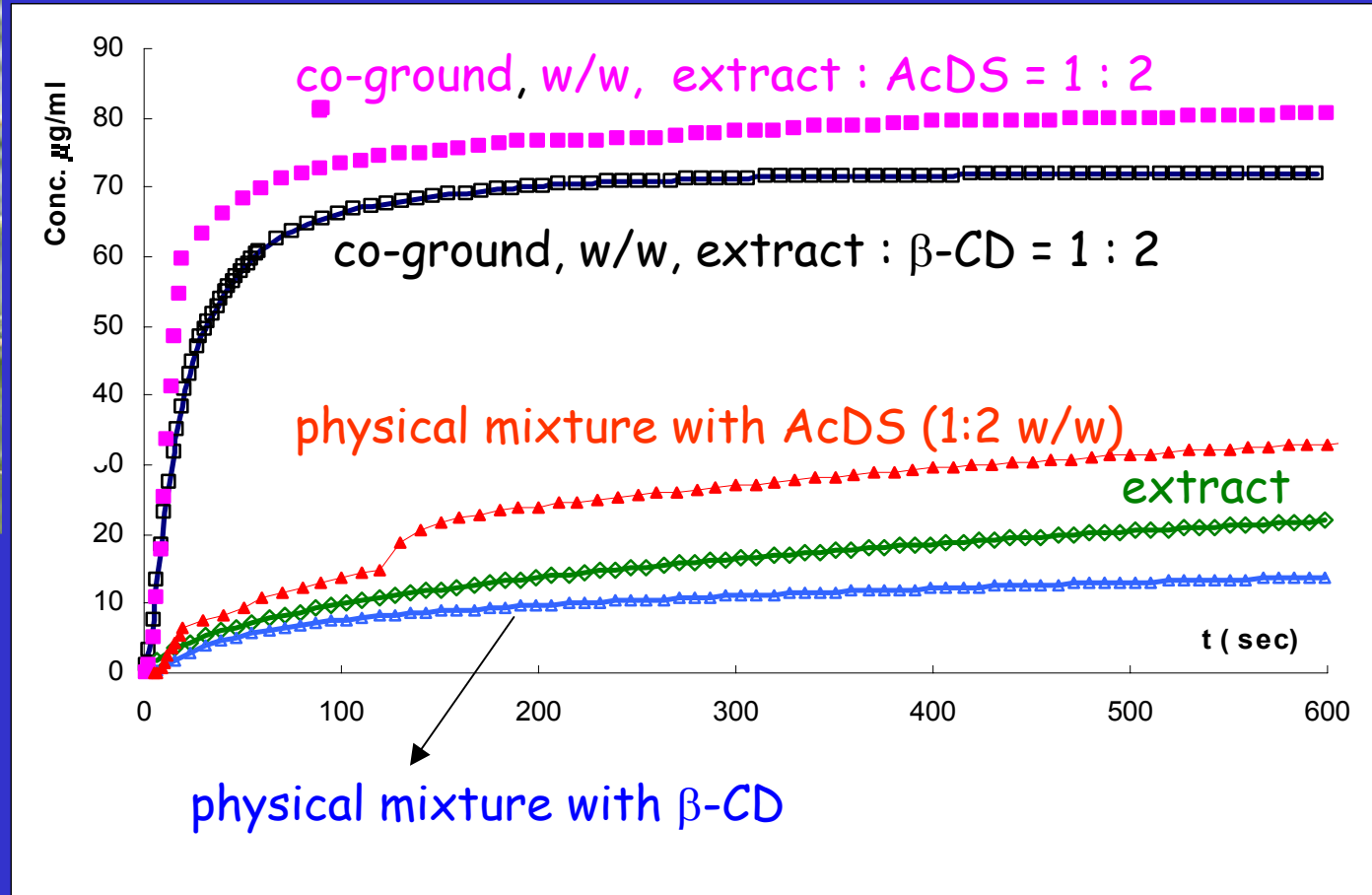
“Which polymers?”

Crosscarmellose



The effect of polymers:
“activation of the solid state”

- Production of partial or total amorphous powders
- Formation of nanocrystals



Medium : Distilled water , $37^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,

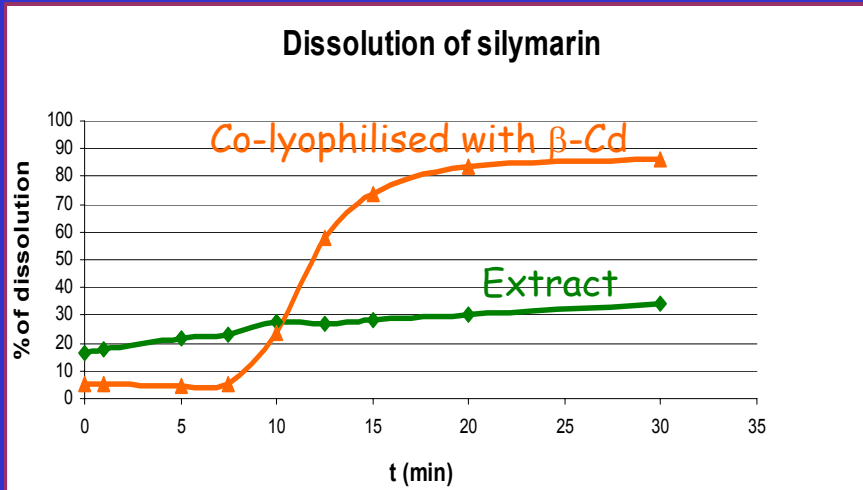
Rotation speed: 50 rev/min

40 mg silybin A+B / 600 ml, $\lambda = 287 \text{ nm}$

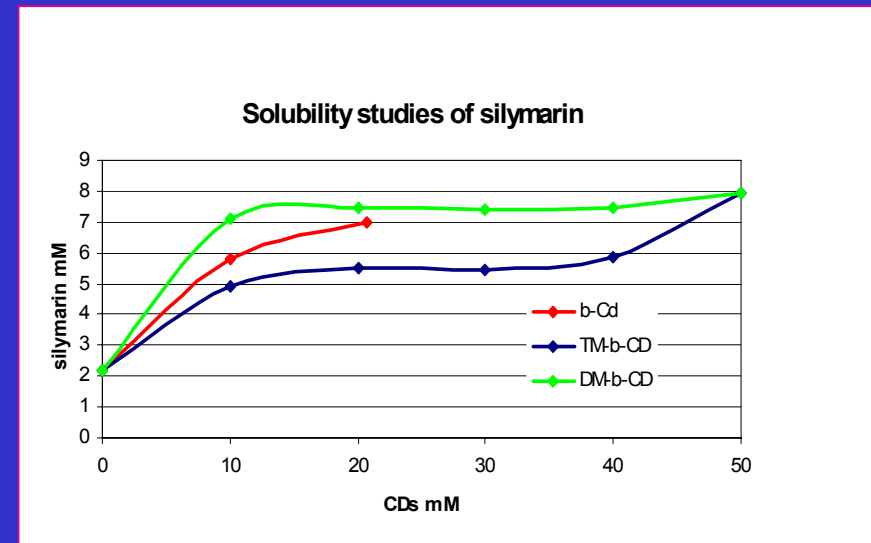
GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“



➤ ...Solubility and rapid dissolution of an API is of superior importance....



Medium : Distilled water , $37^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,
 Rotation speed: 50 rev/min



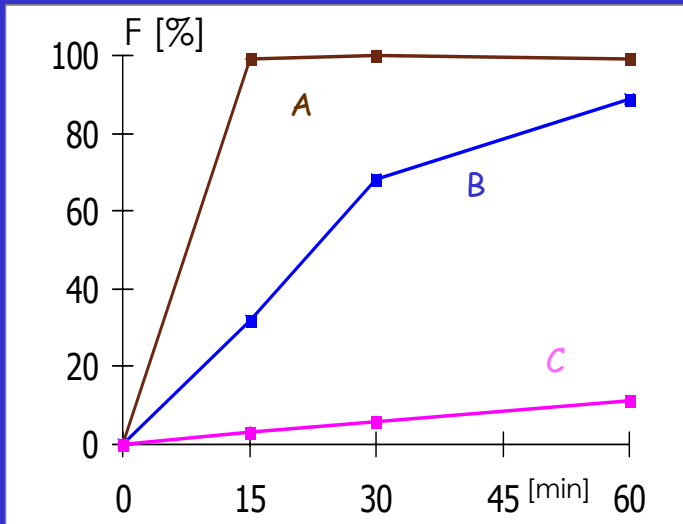
Medium : Distilled water , $27^{\circ}\text{C}\pm 0.5^{\circ}\text{C}$,

GA Workshop of the PC
 „Manufacturing and
 Quality Control of
 Herbal Remedies“

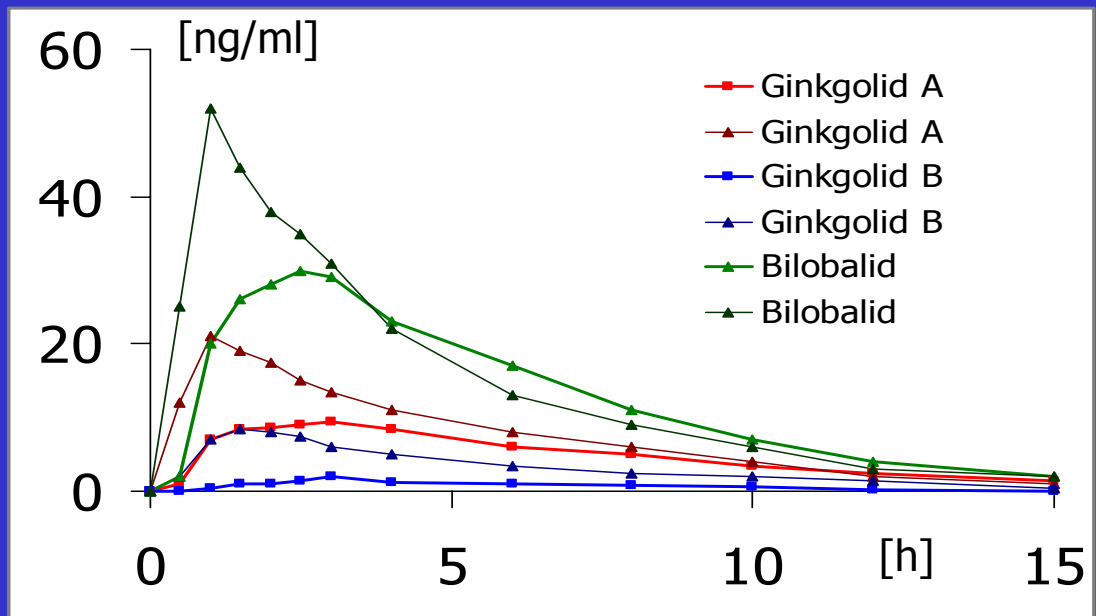


"Formulation impact is significant on the absorption"

Total Terpenlactones/50
rpm/pH 1 (HCl)



In vivo behaviour of product A vs. product B



S. Kreßmann: Thesis, Univ. Frankfurt/M., 2002

GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“



Selection of dissolution media

Standard compendial media

- Distilled Water
- Buffers at different pH
- Simulated Gastric Fluid according to USP 25b
- others

Biorelevant media (Gallia et al., Pharmac. Res. 15, 698-670, 1998)

- FaSSIF (to simulate conditions in the fasted state in the proximal small intestine)
- FeSSIF (to simulate fed-state conditions in the proximal small intestine)



Selection of dissolution media

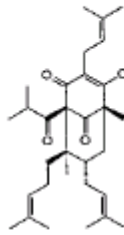
Distilled water is very useful for the Dissolution Kinetic Test

...to differentiate activated mixtures
active substance/polymer
having different "grade of activation"

"it produces information which is useful to discriminate the formulation with an expected better bioavailability"

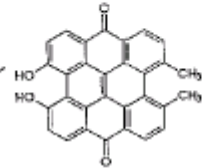
But the reality surrounding HMPs
is more complicated!

Phloroglucinol

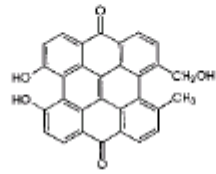


Hyperforin

Naphthodianthrones

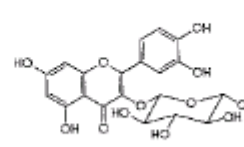


Hypericin

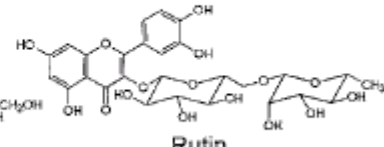


Pseudohypericin

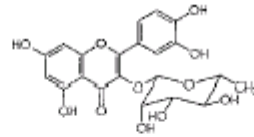
Flavonoids



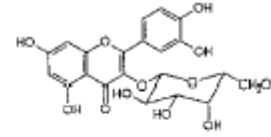
Isoquercitrin



Rutin



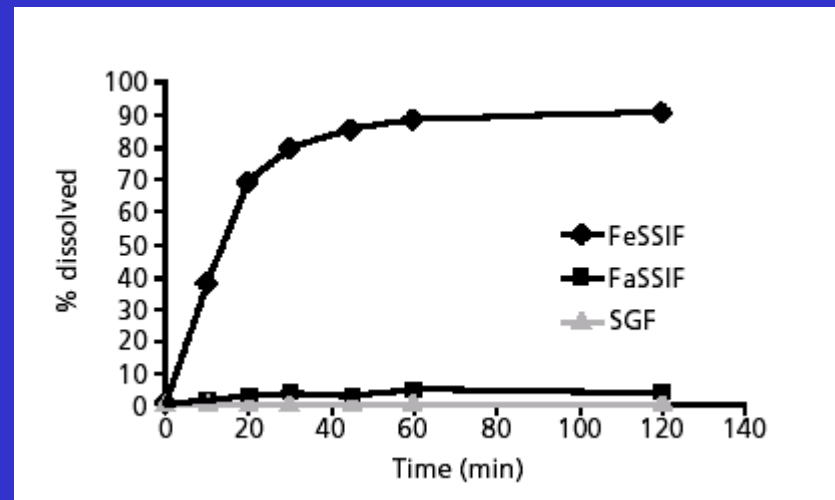
Quercitrin



Hyperoside

lipophil

hydrophil



GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“

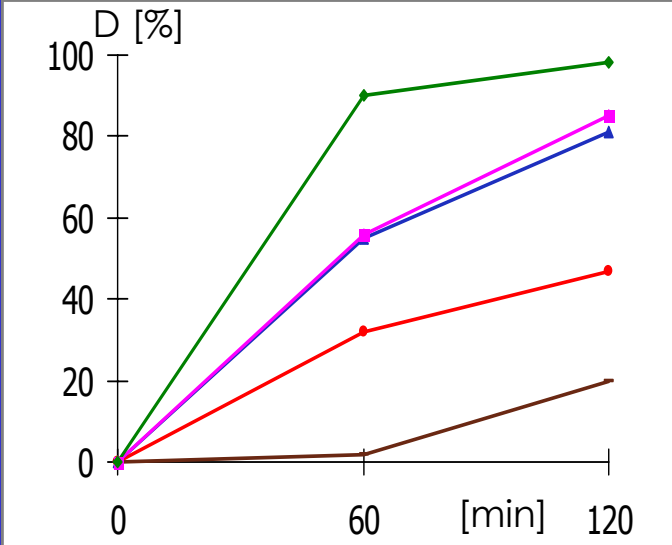


Dissolution profiles
of hyperforin in
different media

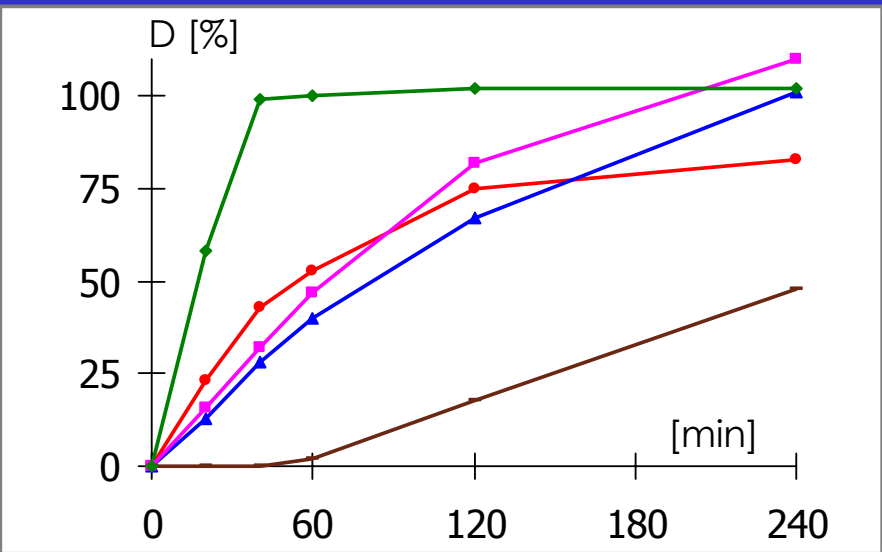
In-vitro dissolution testing (50 rpm)



hyperforin (900 ml FeSSIF)



rutin (900 ml FeSSIF)



GA Workshop of the PC
„Manufacturing and
Quality Control of
Herbal Remedies“



...."Pharmaceutical equivalence does not necessarily imply bioequivalence..."

thus, differences in the excipients or the manufacturing process (or both) can lead to faster or slower dissolution and as a consequence of absorption.

GA Workshop of the PC

„Manufacturing and
Quality Control of
Herbal Remedies“

