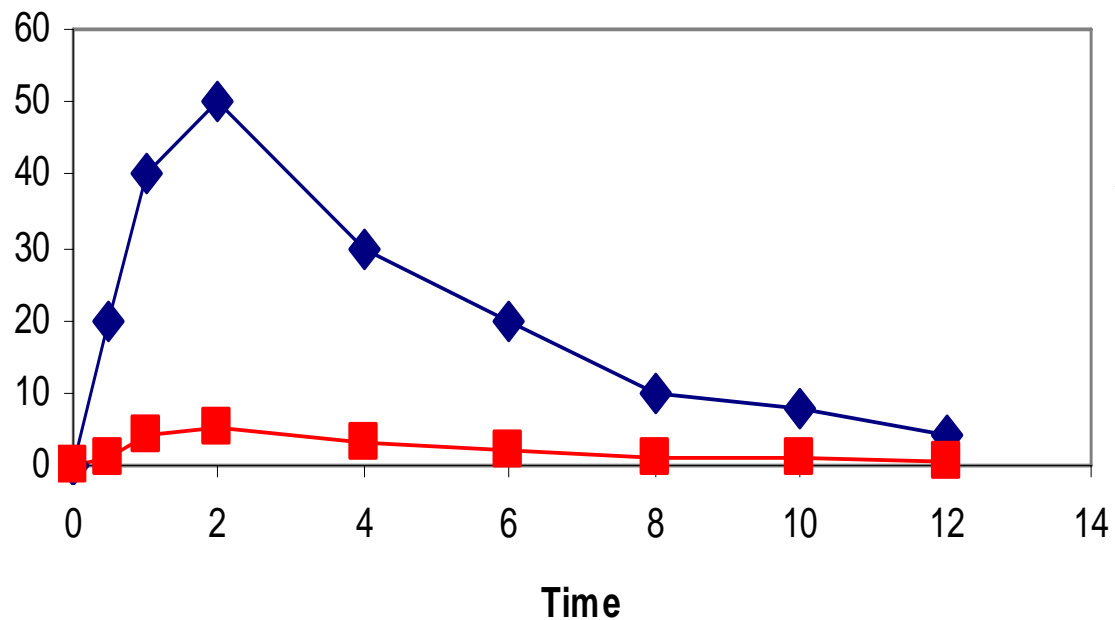


Pharmacokinetics of HMPs

The industrial R&D perspective



Dr. Friedrich Lang
Analytical Development
Dr. Willmar Schwabe
Pharmaceuticals, Karlsruhe



Mit der Natur.
Für die Menschen.

Dr. Willmar Schwabe Arzneimittel
www.schwabe.de

The HMPs scientific area map



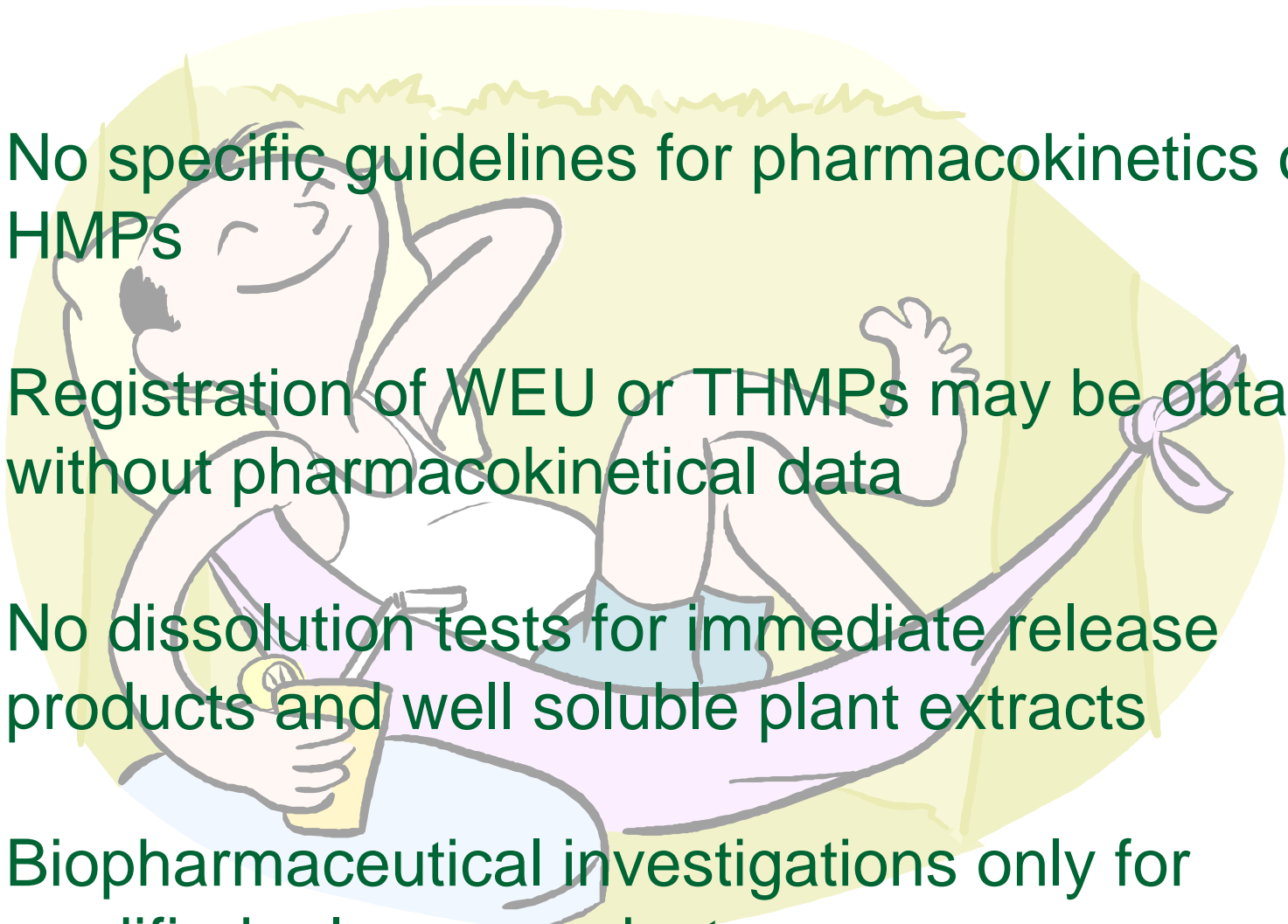
Mit der Natur.
Für die Menschen.

Dr. Willmar Schwabe Arzneimittel
www.schwabe.de

Sit back and relax



Sit back and relax

- 
- No specific guidelines for pharmacokinetics of HMPs
 - Registration of WEU or THMPs may be obtained without pharmacokinetical data
 - No dissolution tests for immediate release products and well soluble plant extracts
 - Biopharmaceutical investigations only for modified release products

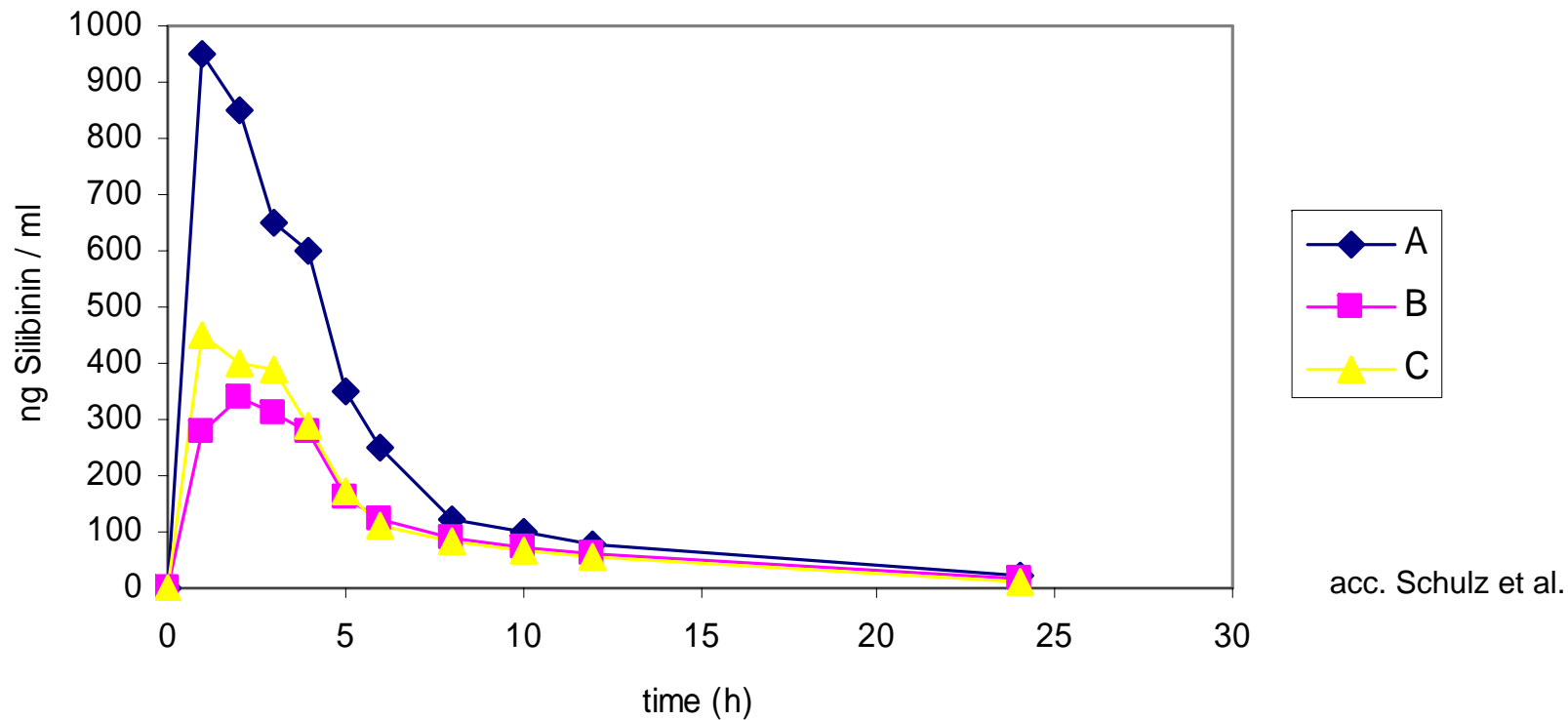
Keep an eye on



Keep an eye on

- Standardised or quantified extracts (Pharm. Eur.)
- Low soluble extracts
- Potential risk

Plasmas levels of silibinin after application of 3 pharmaceutical formulations A, B, C



Bioavailability of hypericine

- Phototoxicity caused by Hypericine:
- Solubility and bioavailability of hypericine depends on content of tannins,
 - ☞ bioavailability study necessary in case of >1800 mg extract per day and > 1 mg total hypericine per day(BfArM)

High state of alert



High state of alert

Development and registration of new plant extracts
and HMPs

TOXICOLOGY

- GLP toxicokinetic studies demonstrating uptake and absorption in different animal species
- Quantification of exposure
- Similarity and differences across species
- Intended dose in humans
- Metabolism



High state of alert

Development and registration of new plant extracts
and HMPs

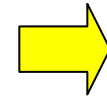
CLINICAL RESEARCH

- Ethics committee, study directors and authorities insist on pharmacokinetics
- Pharmacokinetical questions have to be adressed within the European IMPD formate
- Clinical phase-I studies include pharmacokinetical investigations



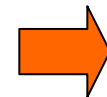
Summary (I)

WEU and THMP



NO pharmacokinetics

Modified release HMPs



SELECTED

biopharmaceutical /
pharmacokinetical
investigations

**Standardised, quantified,
low soluble extracts**



SELECTED

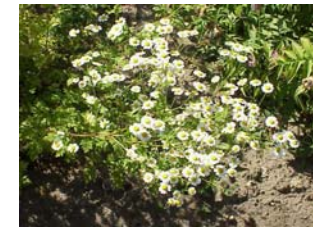
biopharmaceutical /
pharmacokinetical
investigations



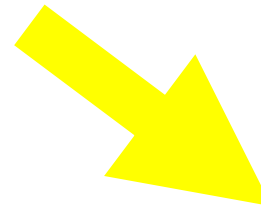
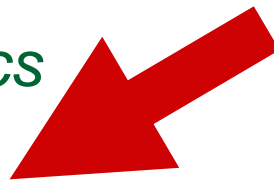
Summary (II)



New plant extracts / HMPs



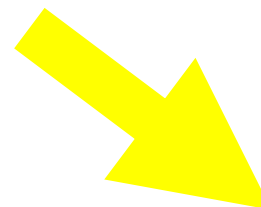
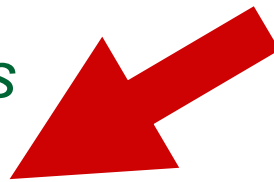
GLP *toxicokinetics*
demonstrating
absorption



Toxicological
interpretation,
metabolites, dose



*Clinical
pharmacokinetics*
demonstrating
absorption /
compliance



Clinical
interpretation,
metabolites, dose

