



**POLITECNICO
DI TORINO**

Department
of Applied Science
and Technology



Ordered Mesoporous Silicas for Drug Delivery in Dermatological Applications

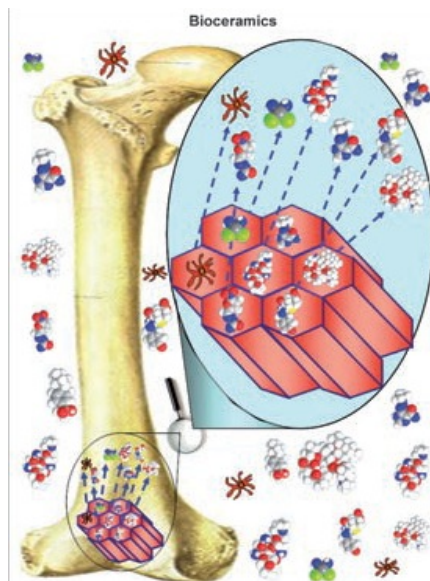
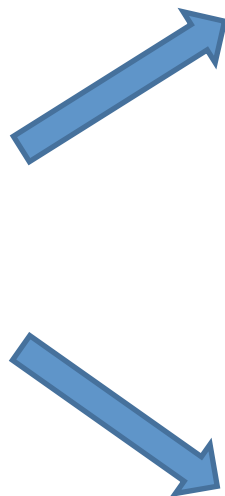
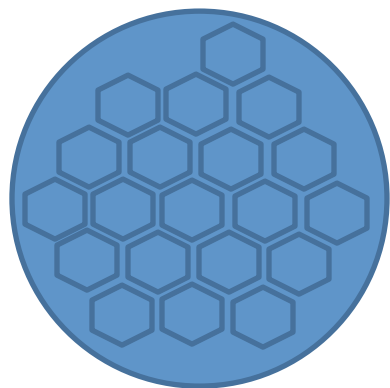
Barbara Onida, R. Mortera, B. Camarota,
D. Caldarola, G. Chierregatti, A. Gignone

NIS colloquium

*"Advances in biomaterials: combining
simulations and experiments"*

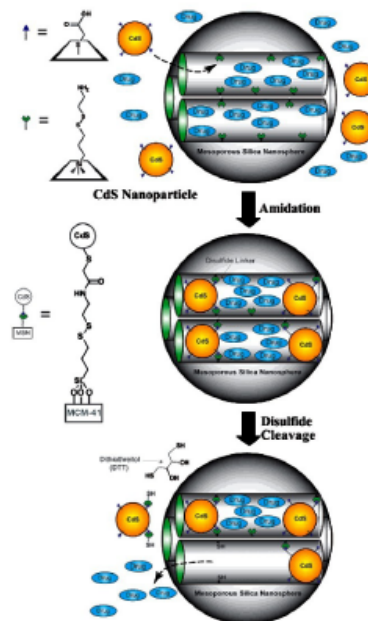
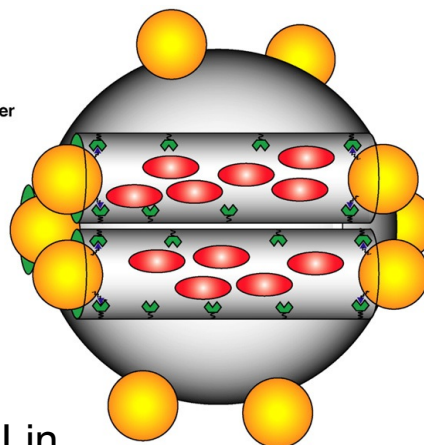
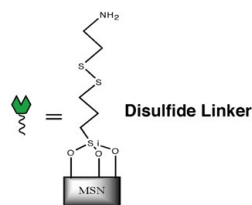
Torino, 28-29 November 2013

OMSSs FOR DRUG DELIVERY



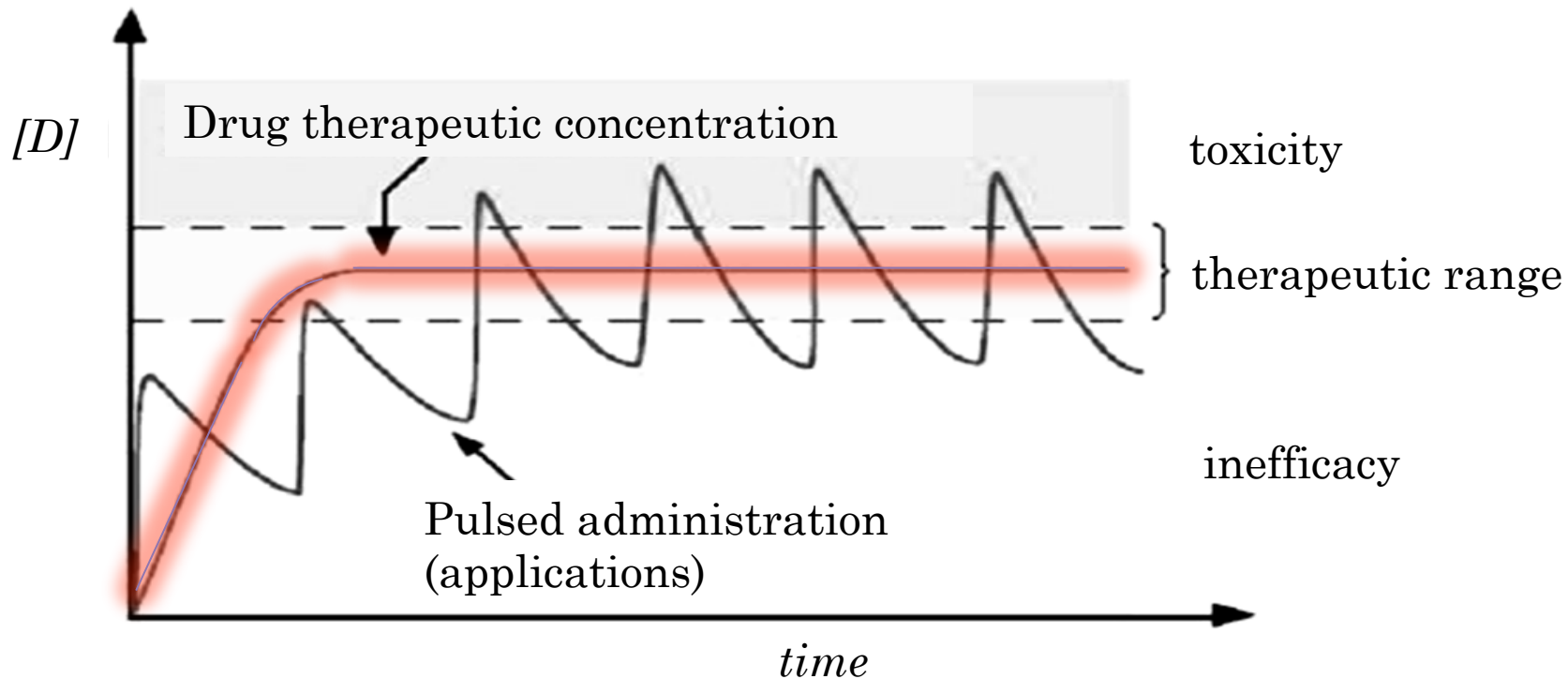
M. Vallet-Regí, *et al.*,
Chem. Mater. **2001**, 13, 308

M. Vallet-Regí, *Chem. Eur. J.*,
2006, 12, 5934.



I. Slowing, J. Vivero-Escoto, C.-W. Wu, V. S.-Y. Lin,
Adv. Drug Delivery Rev., **2008**, 60, 1278.

THE AIM OF THE STUDY



Products for topical applications on epidermis or mucosa allowing constant therapeutic concentration of the Active Principle Ingredient (API) during controlled time (from hours to days) on the application site, so reducing the number of applications.

POSSIBLE TOPICAL APPLICATIONS

- dermatitis, eczema, psoriasis (corticosteroids, NSAIDs)
- Mucosites: 30-40% of chemo-radio therapy patients (antimicrobials, antifungals, antivirals).
- WOUNDS, SORES, BURNS (**ANTIBIOTICS**, ANESTHETICS)
 - low vascularization (poor effectiveness of systemic antibiotics)
 - infection, also related to the medication, is an important issue
 - **higher efficacy**
 - **better patient compliance**



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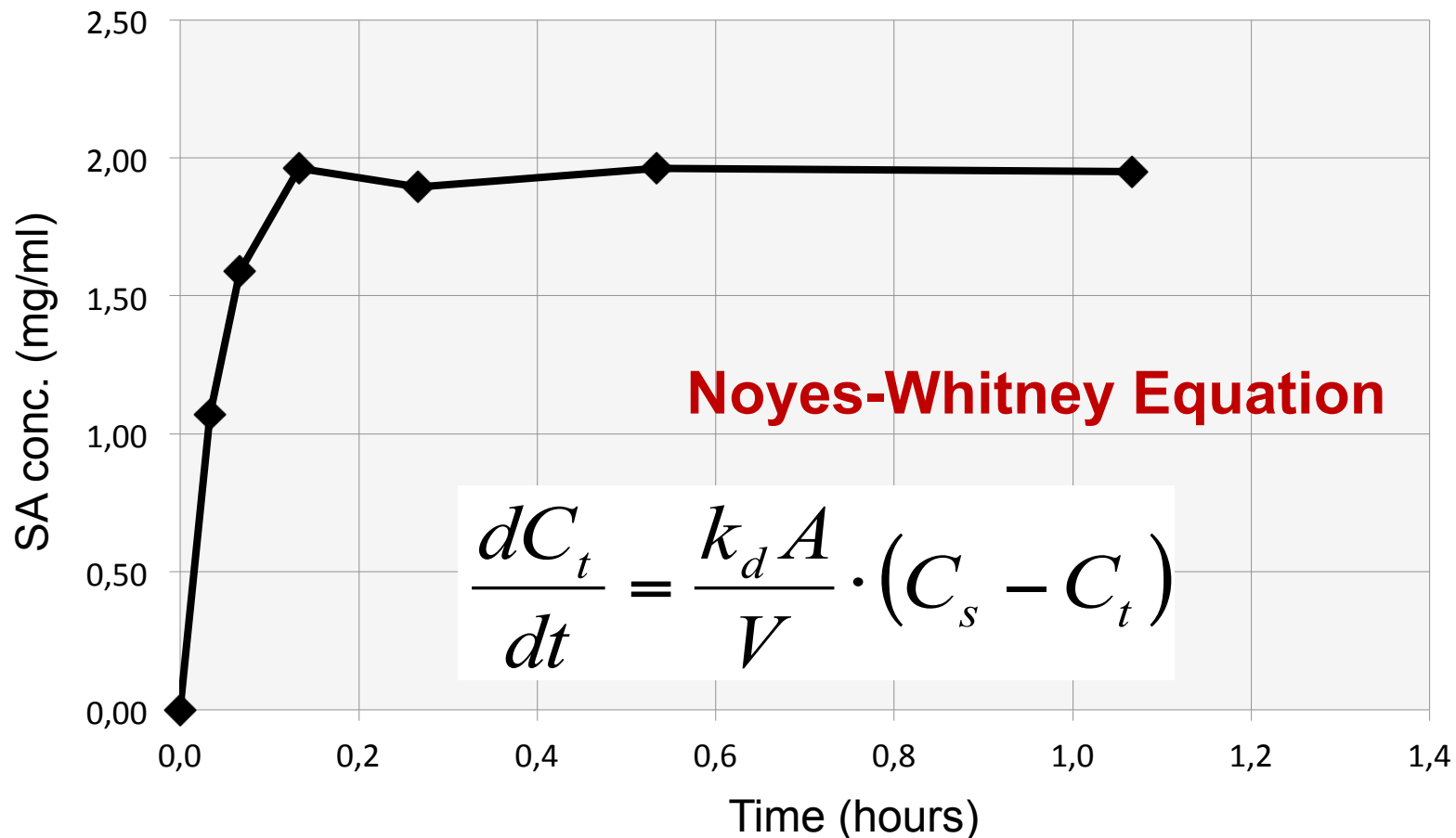
WHY AMORPHOUS SILICA?

- Amorphous silica particles are widely used in cosmetics.
 - Colloidal silica in spray is a source of silicon for the epidermis.
- 
- Silicon is reported to have beneficial effects on the skin: plastic, trophic, antioxidant.

Seaborn CD, Nielsen FH, "Silicon deprivation decrease collagen formation in wounds and bone, and ornithine transaminase enzyme activity in liver." *Biol. Trace Elem. Res.* 2002; 89 (3): 251-61.

Salycilic Acid release from MCM-41 in water

The release may be described as a drug DISSOLUTION by the Noyes-Whitney equation



Noyes-Whitney Equation

(M. Gibaldi et al. *J. Pharm. Sci.* **1967**, 56, 1238
N.V. Mulye et al. *Drug. Dev. Ind. Pharm.* **1995**, 10, 2599)

$$\frac{dC_t}{dt} = \frac{k_d A}{V} (C_s - C_t)$$

C_t is the salicylic acid concentration at time t

- C_s is the salicylic acid solubility (2.0 mg/ml @ 20°C)
- V is the liquid diffusion volume (10 ml in the present test)
- k_d is the dissolution rate constant (0.067 cm/h)

$$k_d = D / h$$

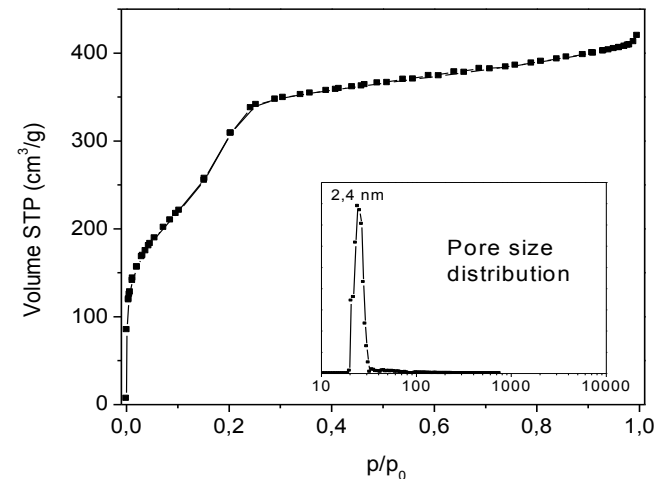
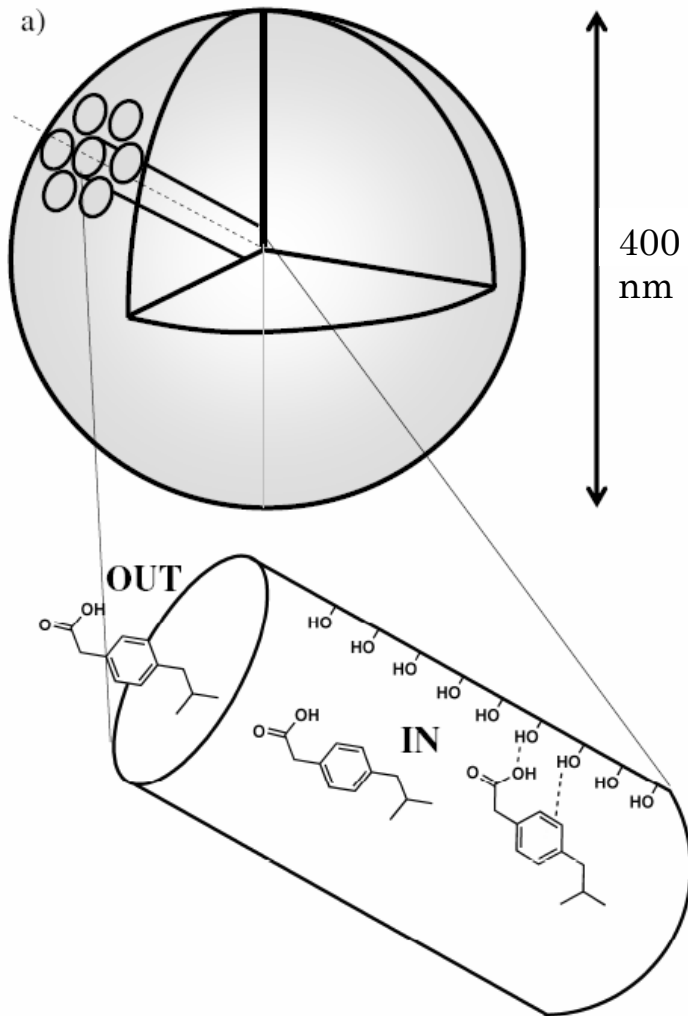
D : diffusion coefficient; h : diffusion layer thickness (l_{pores})

$$D = D_{\text{water}} \frac{(1 - a/r)^2 (1 - 2.1(a/r) + 2.09(a/r)^3 - 0.95(a/r)^5)}{\tau}$$

Renkin and Curry, *Membrane transport in Biology*, Springer-Verlag **1979**



A is the accessible surface to diffusion: **surface separating the internal mesopore volume and the external solution volume**

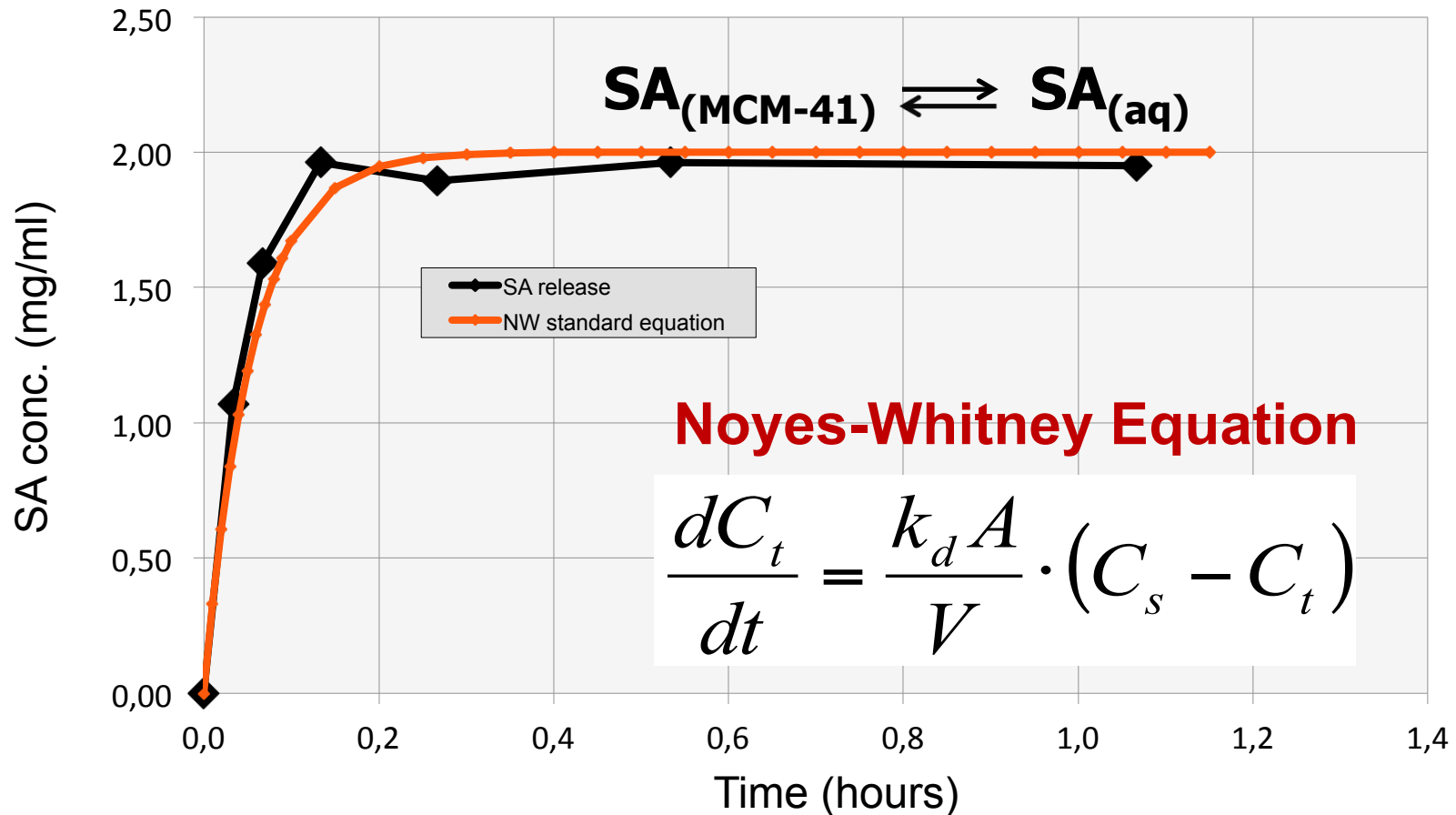


Assuming all particles having the **same diameter** (400 nm) and the **radial disposition of mesopores**

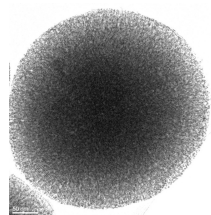
A can be calculated as V_{mes}/l_{pores}



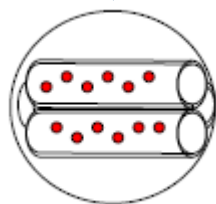
Salycilic Acid release from MCM-41 in water



OMS

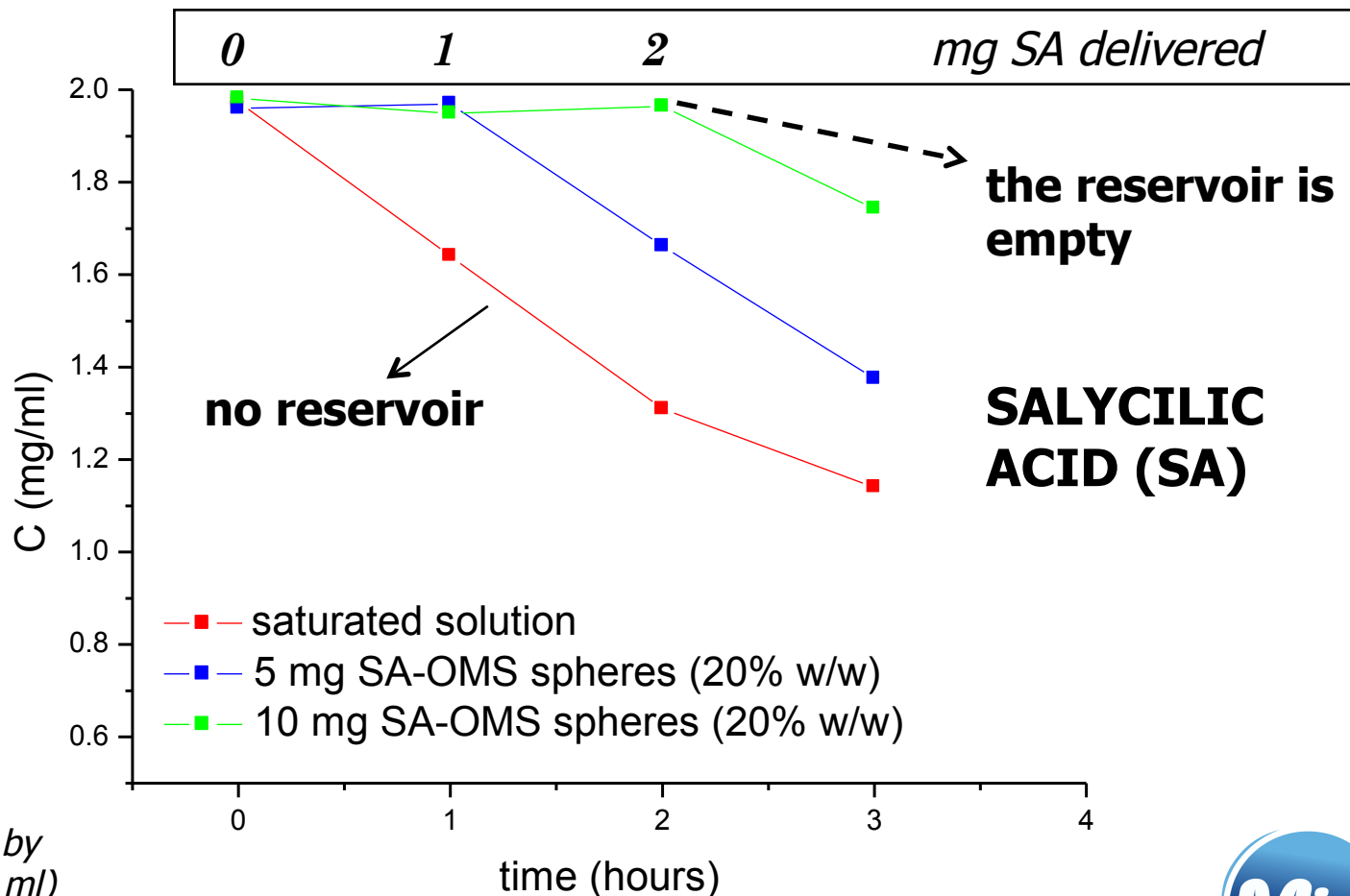


SA
incorporation



SA-OMS

OMS spheres as a DRUG RESERVOIR in saturated solution



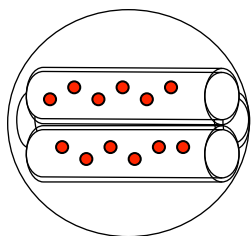
CREAMS OR OINTMENTS FOR PROLONGED DRUG RELEASE AT CONSTANT CONCENTRATION

● Active Principle Ingredient (API)

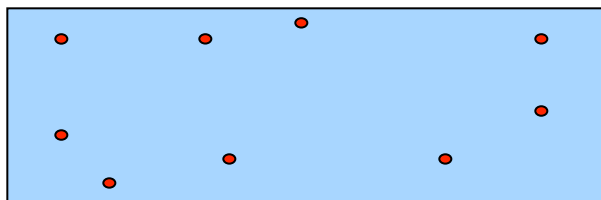
□ Liquid A – API soluble

■ Liquid B – API insoluble

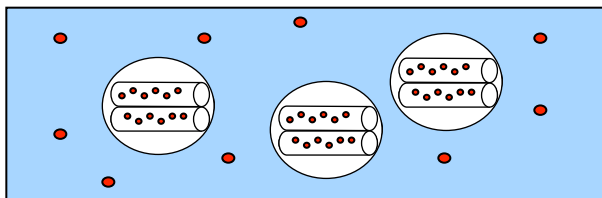
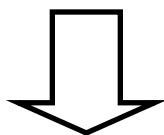
OMS particles



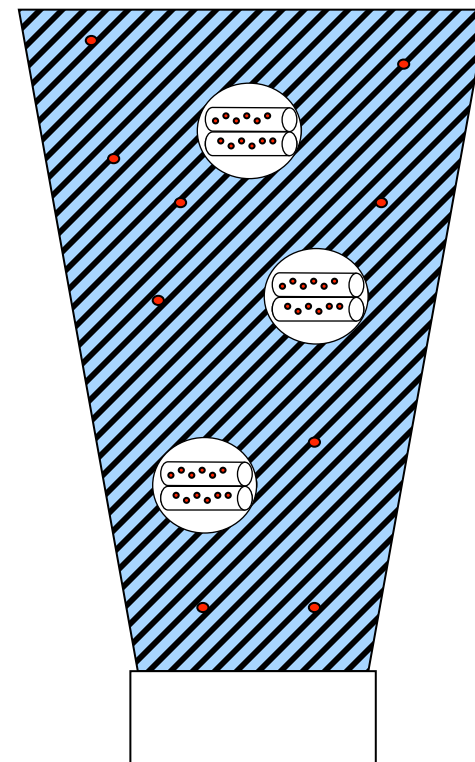
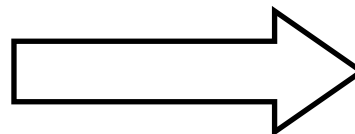
API saturated solution in Liquid A

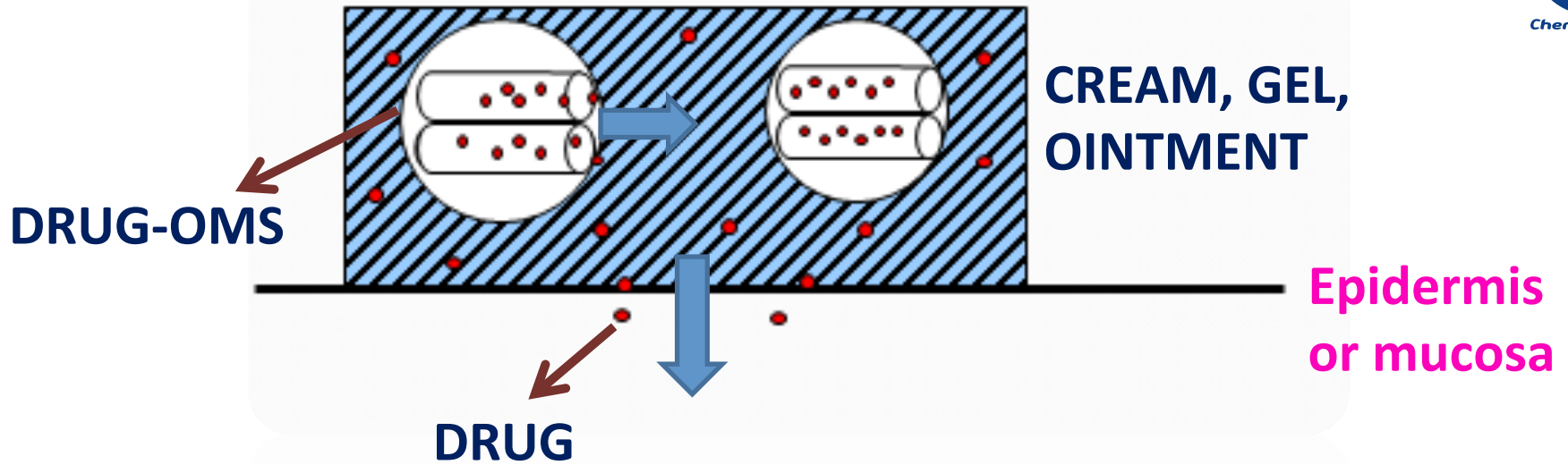


e.g. amikacin in water (45%v/v)-
glycerole (55%v/v) : 5% w/w API

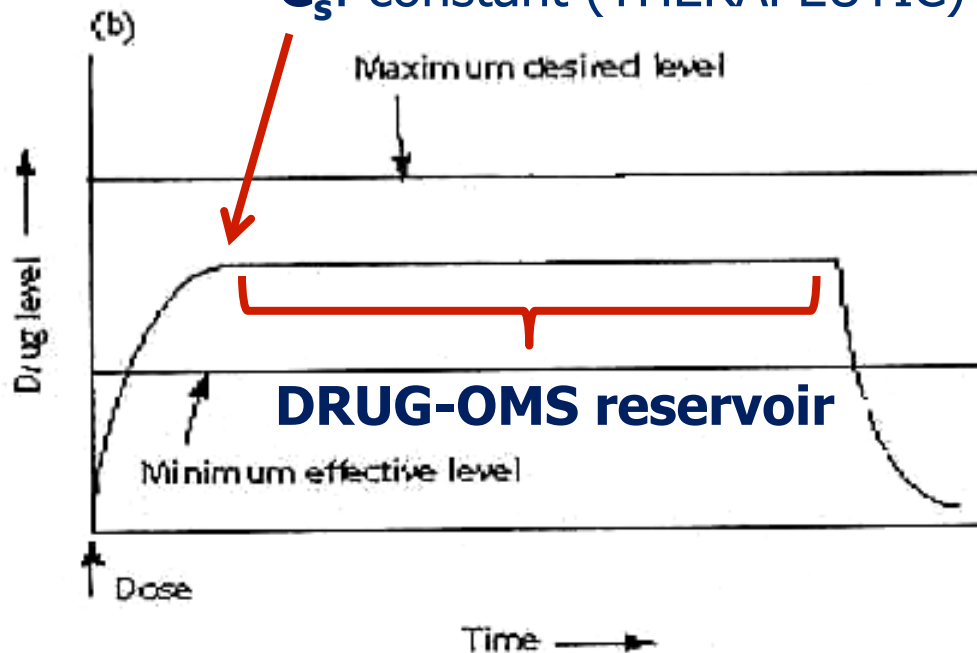


Liquid A + Liquid B





C_s : constant (THERAPEUTIC) concentration on the epidermis



**SUSTAINED
DRUG RELEASE**

CONCLUSIONS

- Ordered Mesoporous Silica particles are excellent host for drug molecules in topical applications, acting as a reservoir in drug delivery.
- In contact with a saturated solution of desired therapeutic concentration, they allow to maintain a constant concentration for a controlled time.
- Creams, ointments or gels containing DRUG-OMS can be formulated in order to achieve a sustained release of the drug to epidermis or mucosa, so reducing the number of applications.
- The amount of amikacin sulphate absorbed by reconstituted epidermis increases in presence of the DRUG-OMS reservoir.



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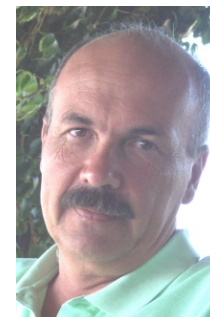
ACKNOWLEDGEMENTS



RENATO
MORTERA



GIORGIO
CHIEREGATTI



DARIO
CALDAROLA



ANDREA
GIGNONE



BEATRICE
CAMAROTA



I3P - Innovative Companies Incubator of the
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