Natural Colour Summit 2013

Exploring how new formulation technologies could improve the properties of natural colours

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A Little About Us

A new company (2012) founded by two experienced industry professionals

Combining diverse experiences, knowledge and wide range of contacts:

…*polymers*, materials science, *chemistry*, imaging, *dyes*, pigments, *emulsion polymerisation*, biocides, *anti-counterfeiting*, environmental, *formulation*, consultancy, *marketing*, business development, *strategy*, regulatory, *training*, events, *R&D*, innovation…

We work with clients *large and small* across different industries which use formulation technology

We help clients by providing and developing new ideas, helping commercialise technologies, project building, consultancy, workshops, contacts and **training**.

…*pharma*, food, *cosmetics*, detergents and cleaners, *coatings*, inks, *agrochemicals*, disinfection etc…

Benefit from translation opportunities from one industry to another → Open Innovation Roadshows

Working in support of major UK national initiatives in *formulation science and technology*.

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Formulation: Opportunities to Translating Ideas *Across* Industries

Formulation technology used in many industries

- Food, cosmetics, pharma, pesticides, coatings, inks, detergents etc.
- Complex products: Multiple ingredients and phases.
- Importance of controlling and measuring product microstructure
- Particles, emulsions, dispersions, gels, microcapsules

But historically, a low tendency to look outside own industry

- Formulation is learned empirically within companies and industries

In formulation, ask yourself the questions

- Who outside your industry might have a similar challenge?
- How have they tackled the challenge?

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Formulation: What Is It Used For In Other Industries?

Making active substance more *soluble / more bio-available*

- Many new pharma actives are low solubility / low availability

Stabilising active substance from *chemical or physical degradation* during product storage or use

- Especially for “biopharma” actives (peptides, proteins) - oral delivery not normally possible

***Improving delivery* of active substance**

- Agrochemical “adjuvants” to enhance coverage and penetration of leaf

***Controlling the release* of a substance**

- Slow release of agrochemical pesticides over time
- Delay release of pharma active until right part of GI tract

***Making actives compatible* with rest of formulation**

- Emulsification of oil soluble ingredients in cosmetics

***Taste masking* in pharmaceutical formulations**

***Photostabilisation* of pharma formulations**

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Challenges in Natural Colour Formulation: An Outsider's View

Words "Borrowed" From Today's Programme for Natural Colour Summit 2013:

…Looking into the **pH (in)stability** *of blue colors…Exploring a new method to combine natural colors with an edible carrier,* **without surfactants and Aluminium**

Discussing ways of overcoming the challenges of:

Light sensitivity..pH dependency…

Heat sensitivity…

Humidity dependency…

"Discussing natural blues that can be used in the US and ways to overcome the **challenges in application***… Understanding ways of combating the* **sour taste** *associated with using natural blue…*

Understanding the challenges of finding a natural red that is **heat stable** *…Discussing innovative ways of mixing natural red with other ingredients to* **facilitate its use** *in application and* **ensure it remains bright and stable***…*

…looking at the effects of decoration on **stability of colours at different pHs***…*

Reviewing innovative technology to counter **regulations** *of synthetic lakes and* **aluminium salt content***…*

Solubility and Availability: The Challenge in Formulation

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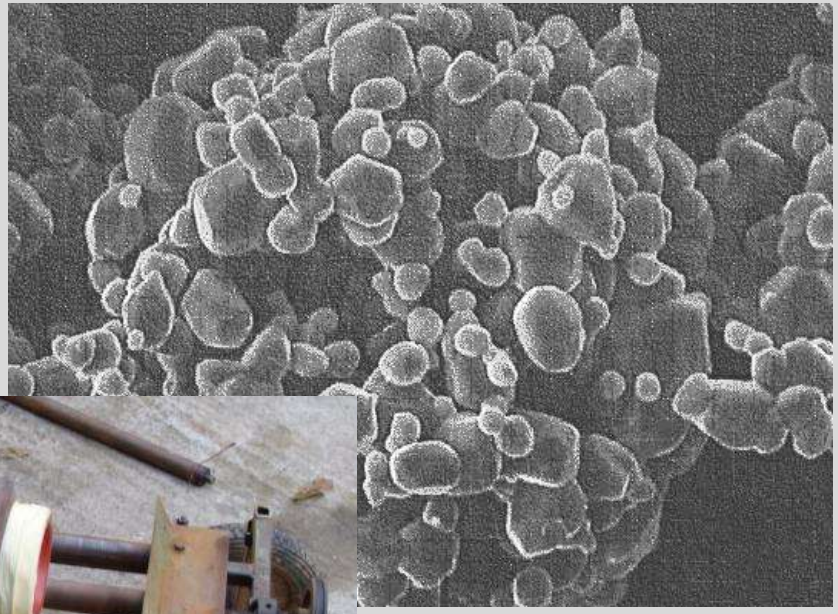
The Old Way: How We Did Particle Size Reduction in the 20th Century



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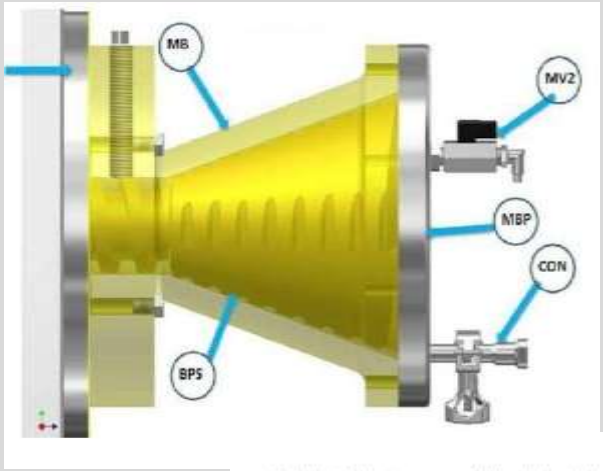
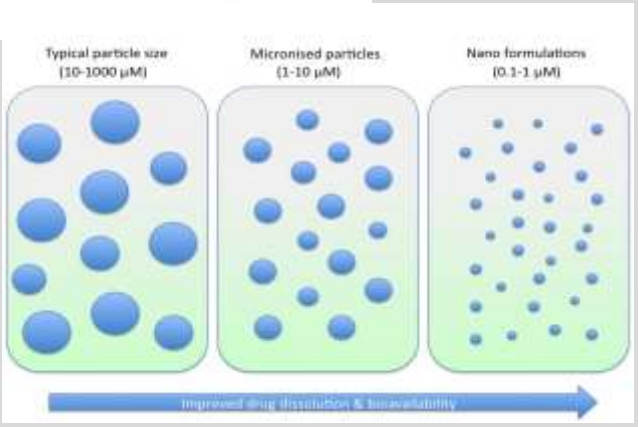
Developments of Established "Top Down" Methods: Nanomilling





lena nanoceutics

Images from http://www.lenanano.com/science-and-technology/technology.html

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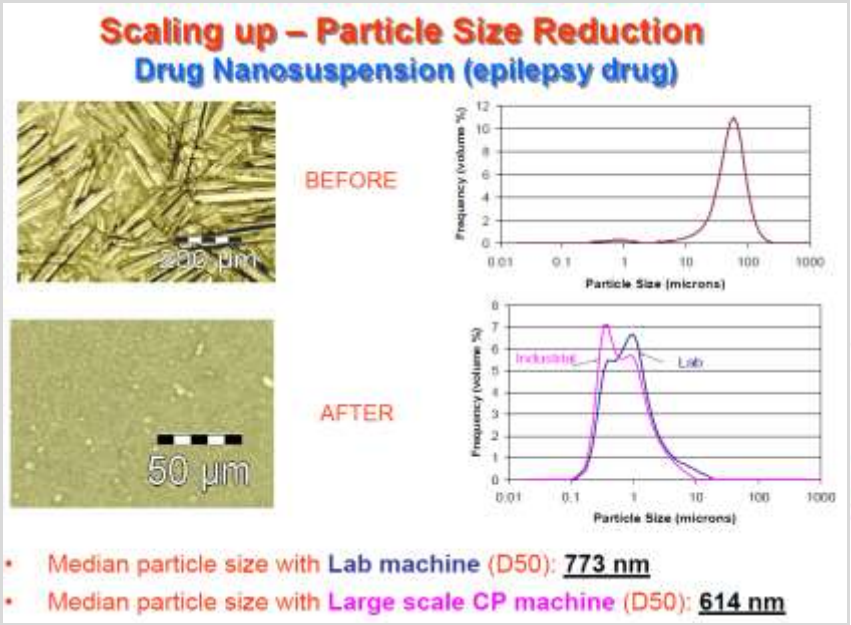
“Top Down” Particle Size Reduction Without Media: Microfluidizer



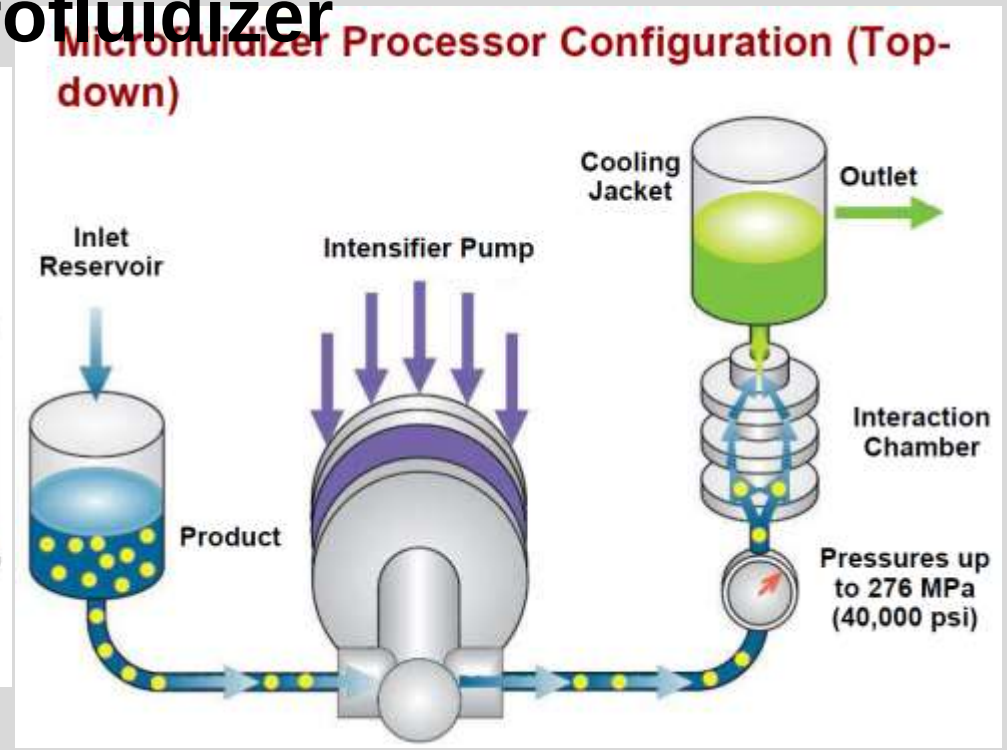


Image from: http://www.bio.huji.ac.il/upload/Cellular_Microfluidizer_Protocols.pdf

Microfluidics

Image from: http://www.microfluidicscorp.com

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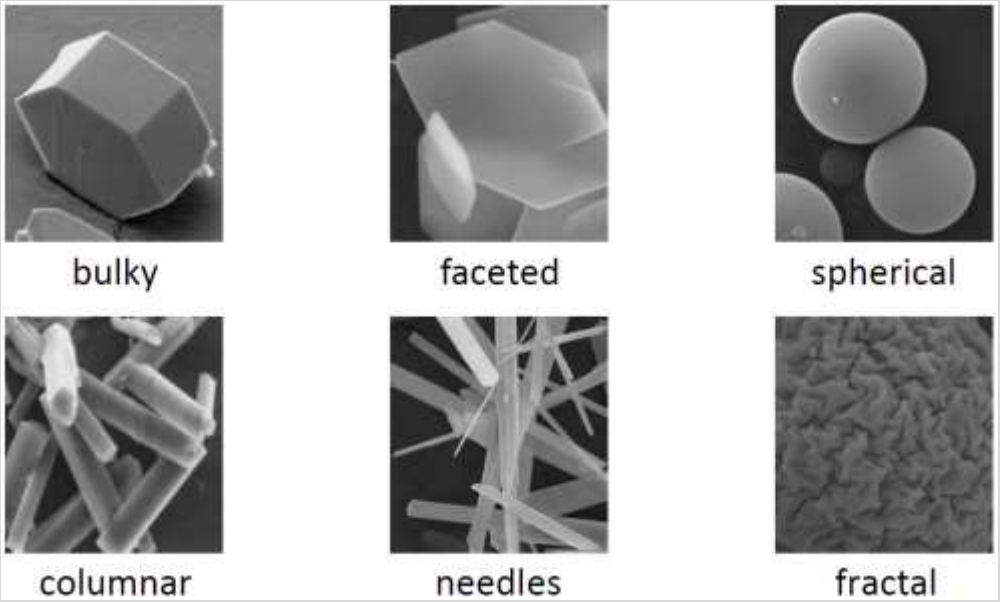
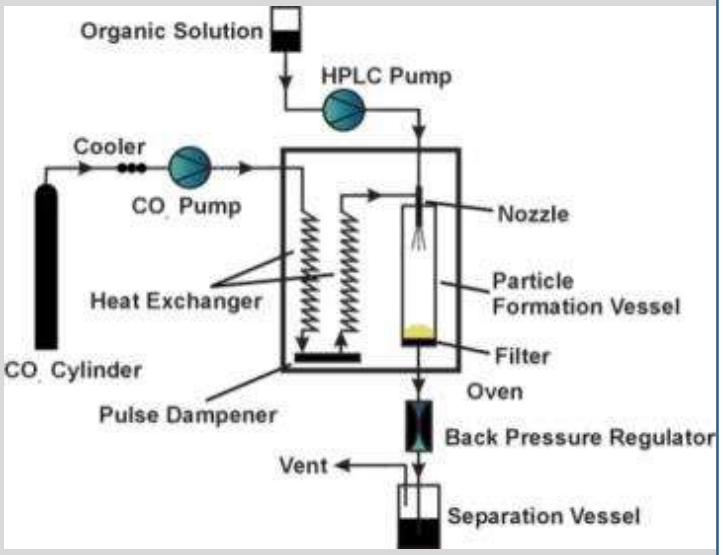
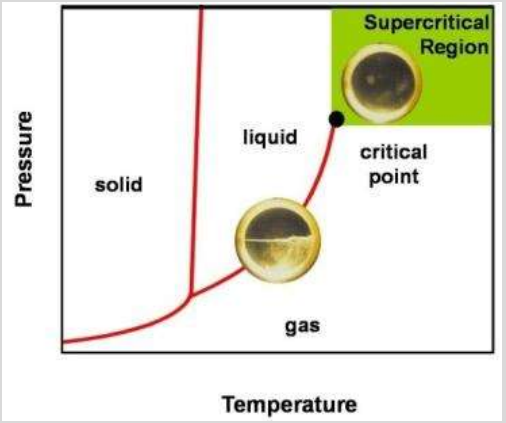
“Bottom-Up” Synthesis for Precise Particle Design





CrystecPharma

Images from http://crystecpharma.com



Supercritical Fluid may be used as solvent or anti-solvent

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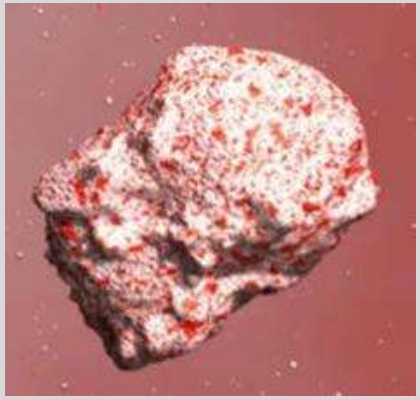
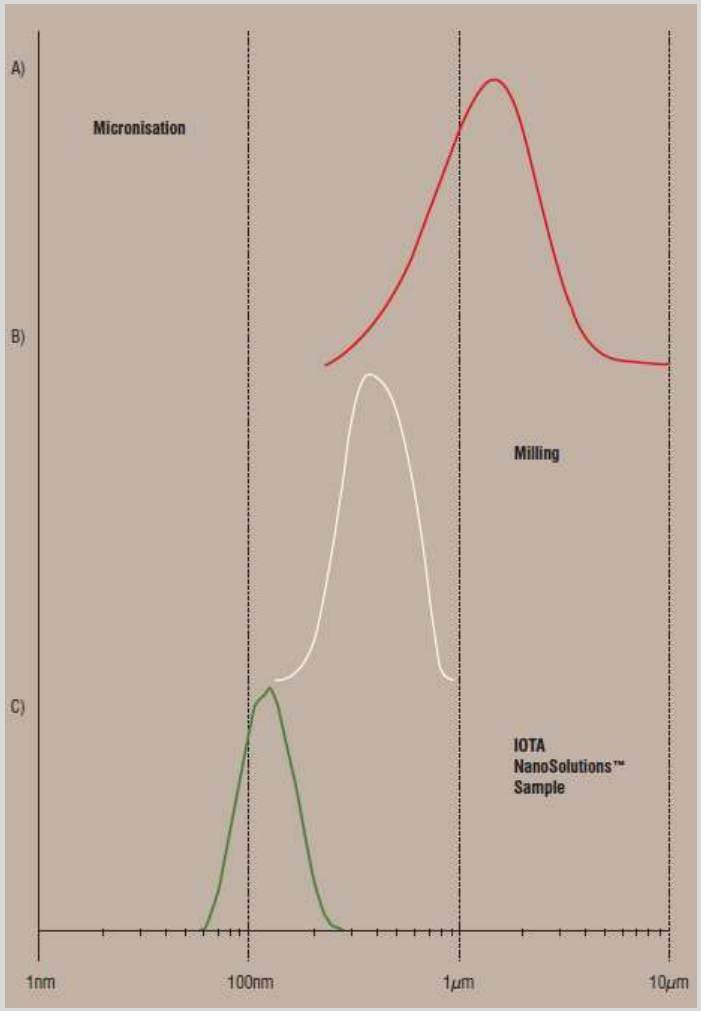
Bottom-Up Particle Design: Synthesise and Formulate in One Step



Low solubility active particles embedded in soluble solid matrix



IOTA NanoSolutions

Images (L & R) from www.iotanano.com
Image (Centre): "Chemistry & Industry" Magazine 25 Jan 2010

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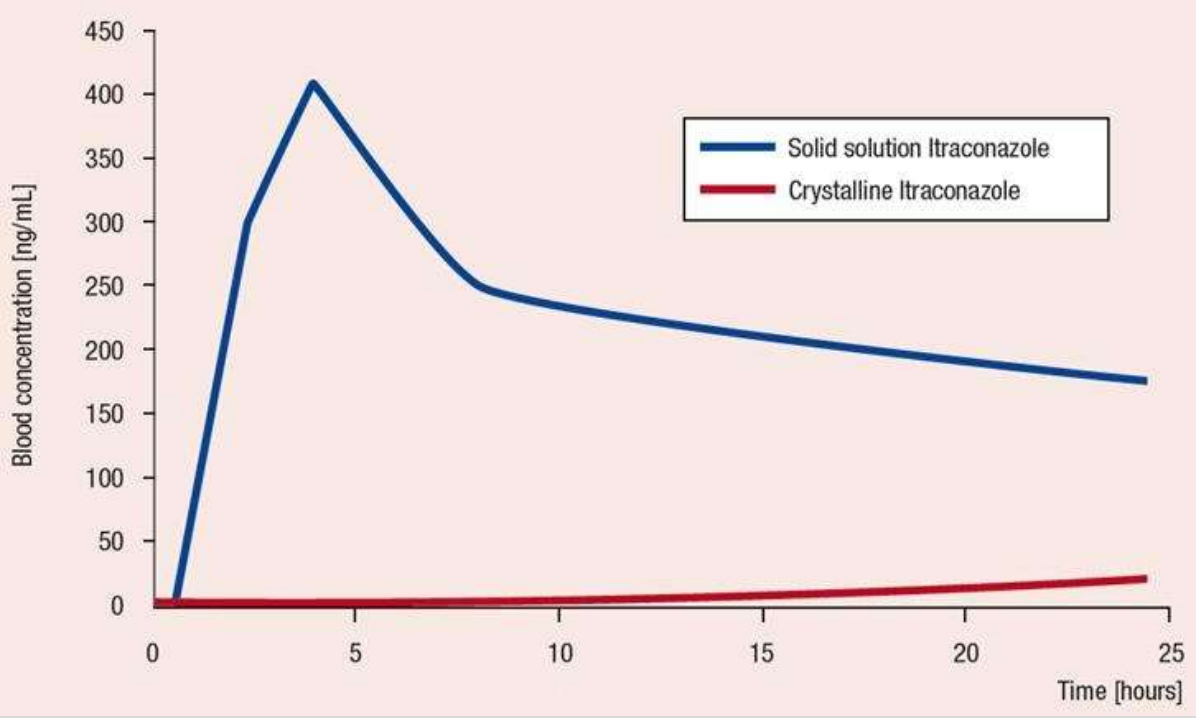
Solubility and Availability: The Challenge in Formulation

Use of Solid Solutions:

- Active is **molecularly dispersed** (not particles) in solid carrier matrix
- Matrix may be water soluble, enhancing dissolution rate of active
- **Solid solutions may be produced via e.g hot-melt extrusion**



BASF Soluplus®

Image from http://www.pharma-ingredients.basf.com/Documents/ENP/Brochure/EN/RZ_BASF_Broschure_Soluplus.pdf

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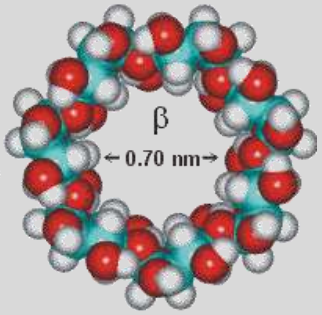
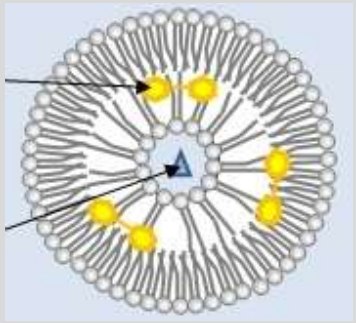
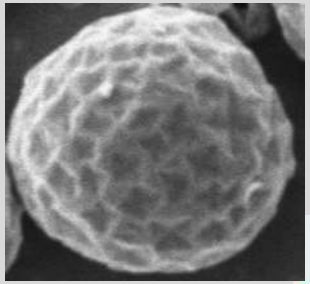
Encapsulation: Not new but in a constant state of development

Why Encapsulate?

- Stability (chemical, heat, light…)
- Formulation compatibility
- Controlled release
- Taste masking







Encapsulation can be

- Molecular
  Cyclodextrins, Calixarenes, Zeolites, Metal organic frameworks etc
- Nano
- Micro
- Macro

Photo: Idea go / freedigitalphotos.net

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Molecular Encapsulation Example: Cyclodextrins – Use in Drug Delivery

Already used e.g for flavours to improve stability

Use in pharma for taste masking, improving solubility, stabilising proteins

Use with carotenoids, curcumin and bixin reported

Used to photostabilise drug actives

"The cavity size of α-CD is insufficient for many drugs and γ-CD is expensive…but the low aqueous solubility…limited the use of β-CD…"

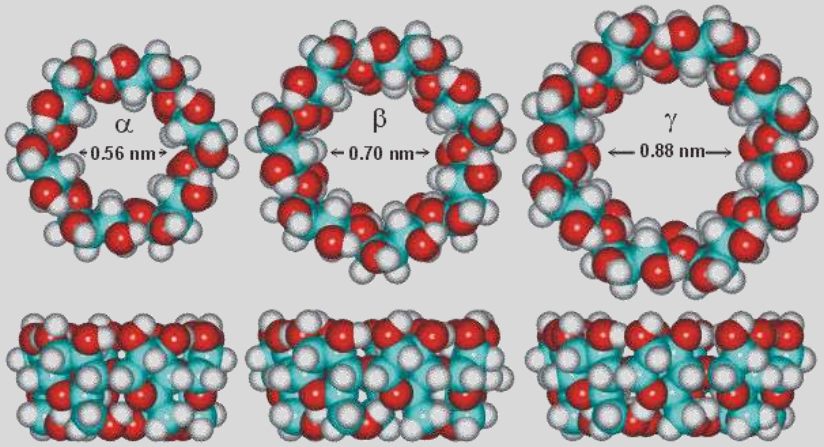

Image: http://www.lsbu.ac.uk/water/cyclodextrin.html

Challa et al AAPS PharmSciTech 2005; 6 (2) Article 43
http://www.aapspharmscitech.org

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Molecular Encapsulation Example: Zeolites – Use in Drug Delivery and Elsewhere

"Zeolites were studied to investigate ability to encapsulate and to release drugs…after activation these materials offer good potential for a modified release delivery system of ketoprofen."

Rimoli et al J Biomed Mater Res, 2008

Association of indigo with zeolites for improved colour stabilization

"Among the three indigo@zeolite systems tested in this study, only the indigo@MFI hybrid presents a conclusive color stability under oxidizing condition."

Dejoie et al, Applied Spectroscopy 64, 10 (2010) 1131-1138

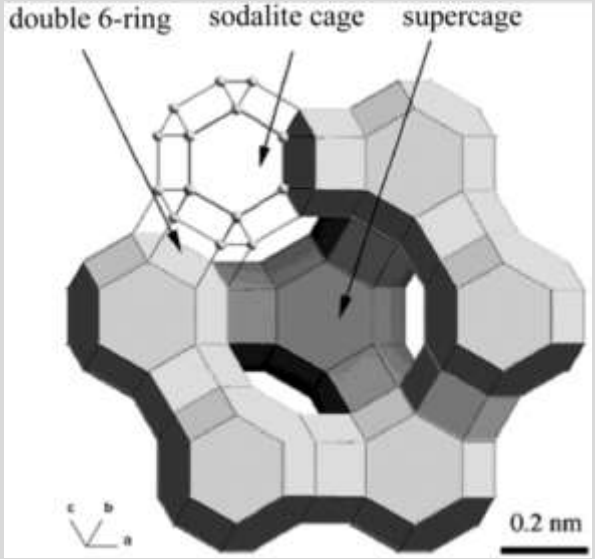

Image: www.intechopen.com

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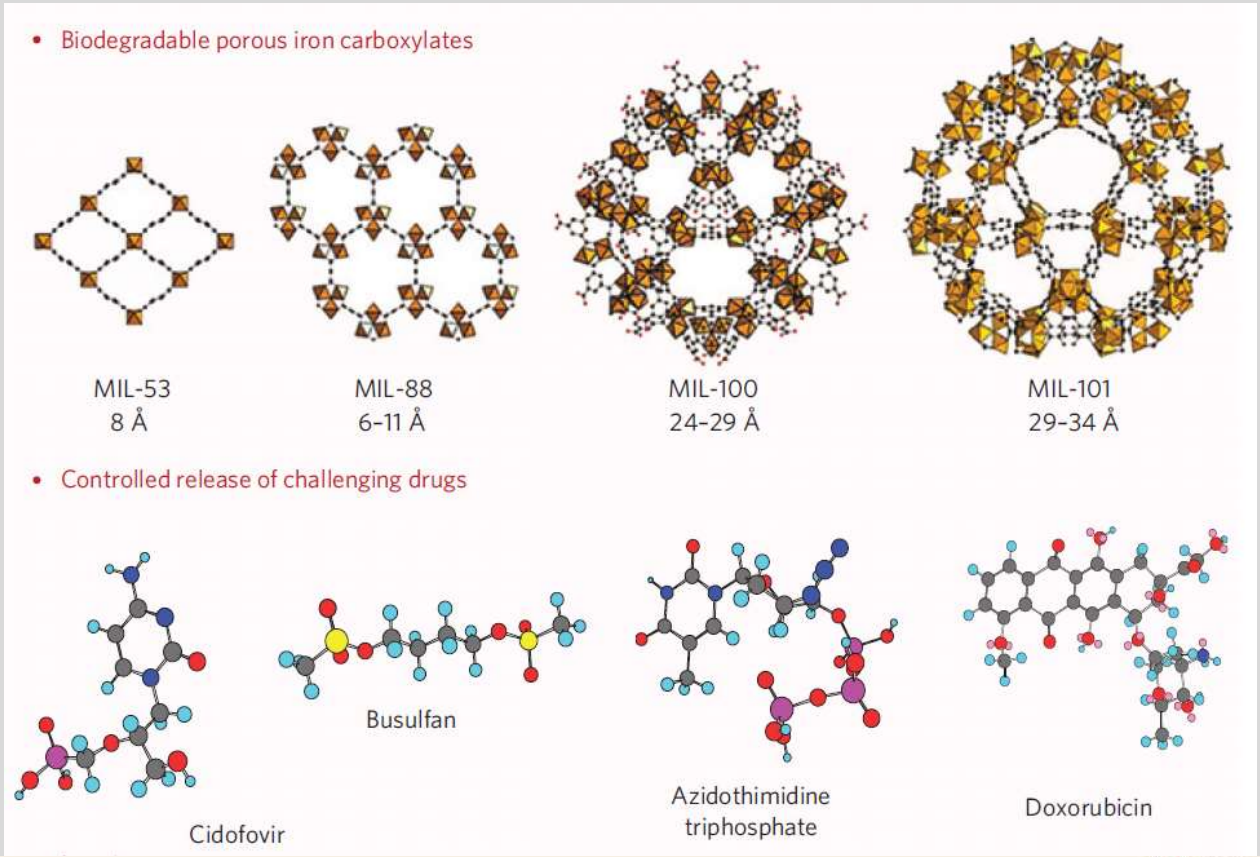
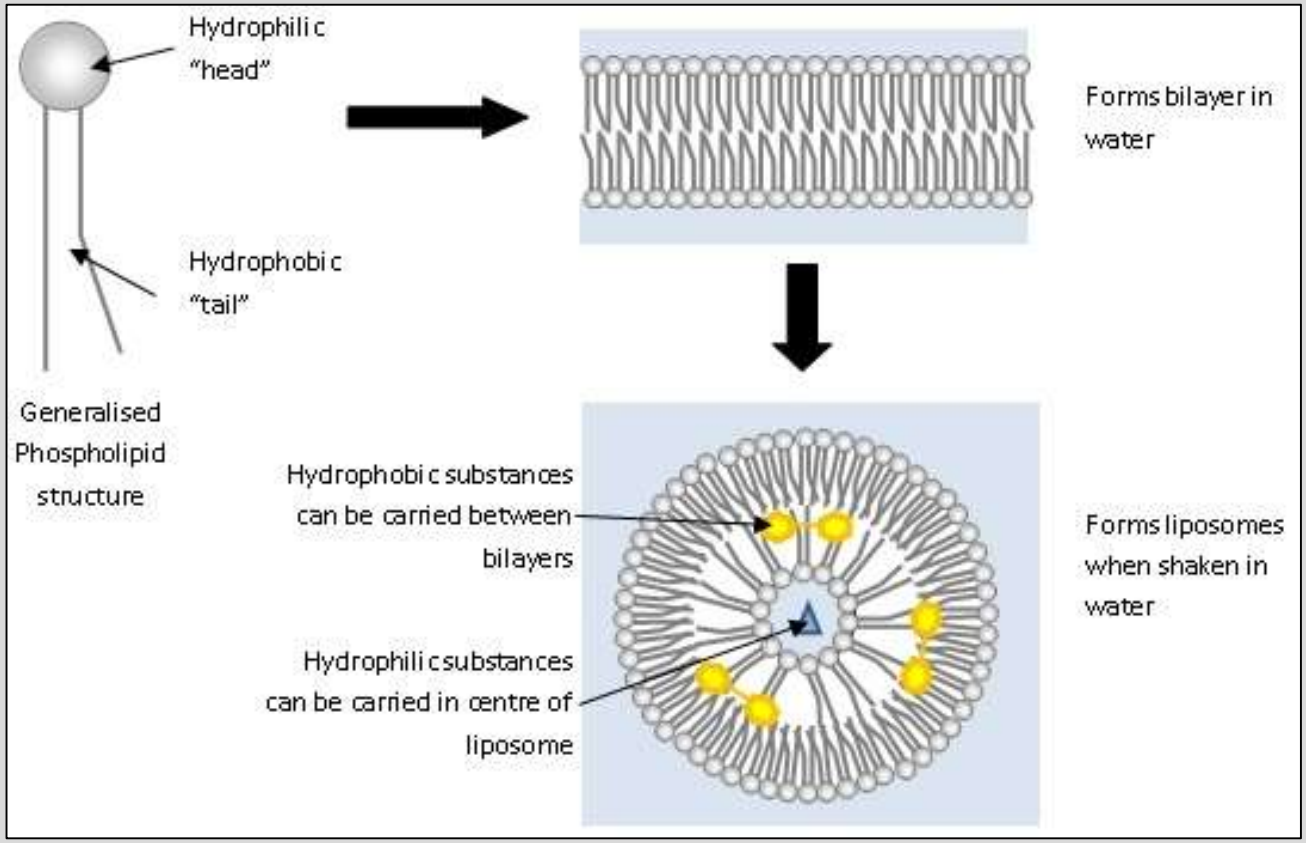
Molecular Encapsulation Example: Metal Organic Frameworks – Use in Drug

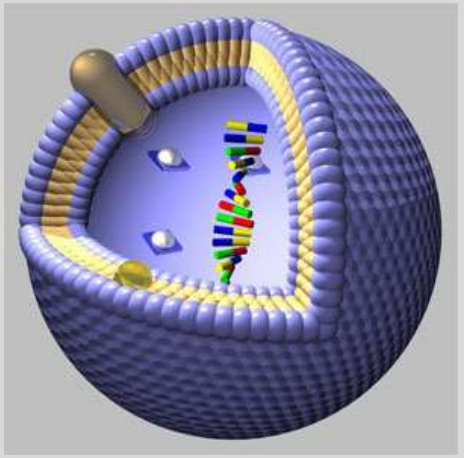


Images:
Horcajada et al,
Nature Materials,
Vol 9, Feb 2010
p172

Organic linker	Muconic acid	Fumaric acid	Trimesic acid	Amino terephthalic acid	Terephthalic acid
Crystalline structure					
Flexibility	Yes	Yes	No	No	Yes
Pore size (Å)	11	6	25 (5.6) 29 (8.6)	29 (12) 34 (16)	8.6

Nanoencapsulation Example: Lipsomes – Use in Drug Delivery





Yvonne Perrie, Aston Univ:
Phospholipid based liposomes for oral vaccine delivery
www1.aston.ac.uk/lhs/staff/az-index/perrie

Image: http://www.di.uq.edu.au/proj5background (University of Queensland)

Aston University Life & Health Sciences

vbi

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Nanoencapsulation Example: Lipsomes – Use in Drug Delivery

Lipsomes can enable delivery through barriers due to incorporation of phospholipids

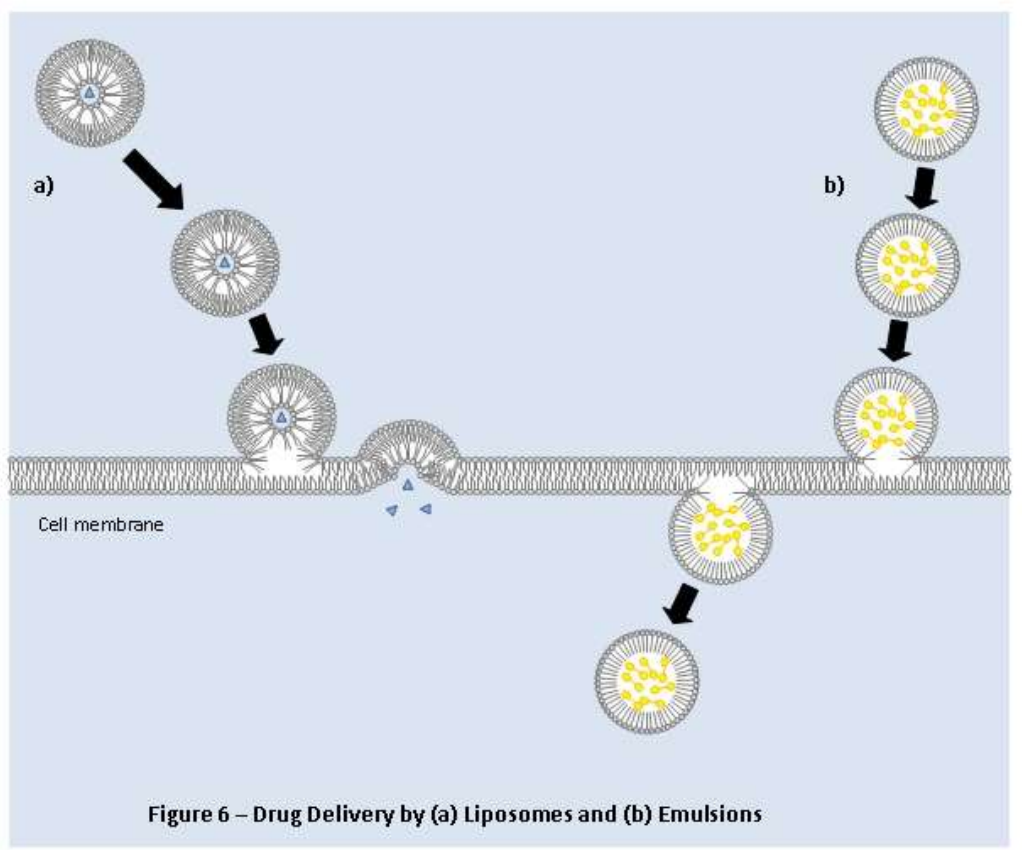

Figure 6 – Drug Delivery by (a) Liposomes and (b) Emulsions

Image: http://www.di.uq.edu.au/proj5background (University of Queensland)

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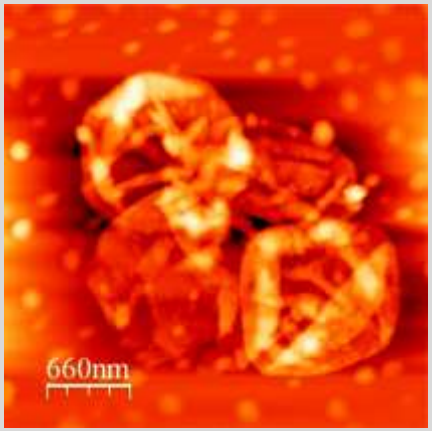
Nano- to Microencapsulation Example: Core Shell and Controlled Release



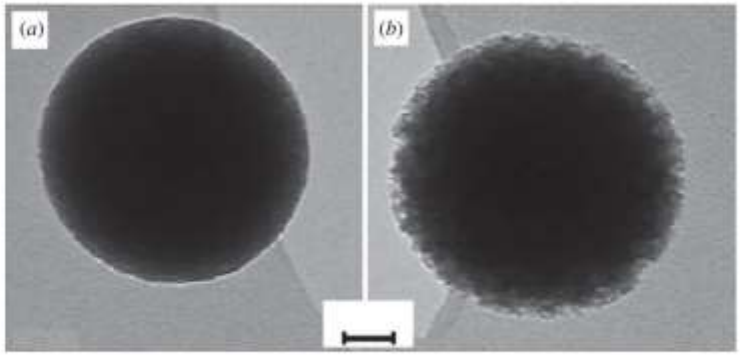


Figure 9. (*a*) TEM image of a 250 nm silica particle coated with a 50qPDMA-PDEA micelle monolayer. (*b*) A single 250 nm silica particle following deposition of four alternating 50qPDMA-PDEA and PDEA-PMAA micelle layers. Scale bar, 50 nm.

Addison et al, *Phil. Trans. R. Soc. A* (2010) **368**, 4293–4311

Block co-polymer micelles deposited on latex or silica particles

- Stable to laundry wash cycles
- pH triggerable release of actives?

"It has been shown that **block copolymer micelles** can selectively encapsulate and release hydrophobic materials; therefore, the incorporation of such responsive species within films has the potential to offer increased functionality. "

Addison, Cayre, Biggs, Armes & York: *Langmuir*, 2008, *24* (23), pp 13328–13333
Phil. Trans. R. Soc. A (2010) **368**, 4293–4311

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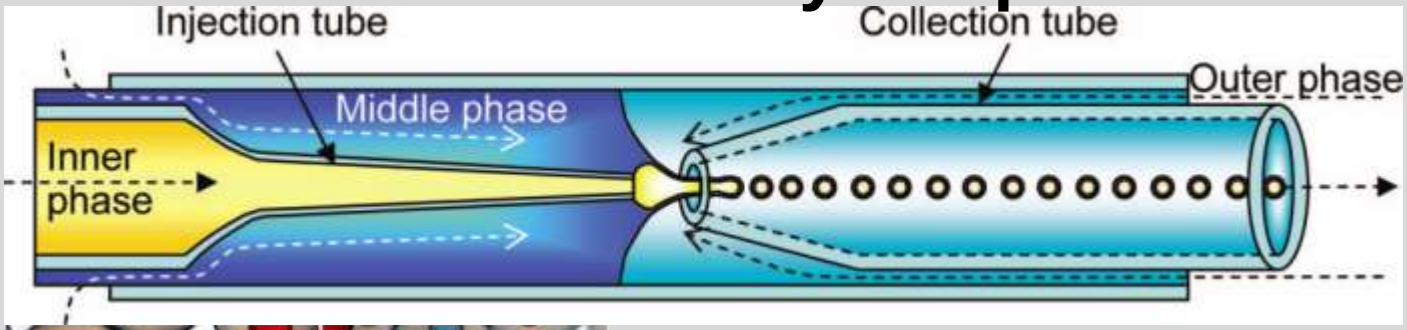
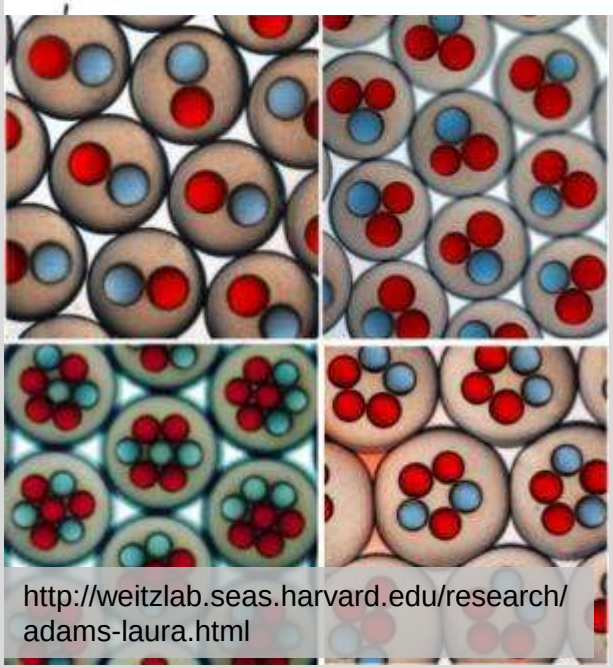
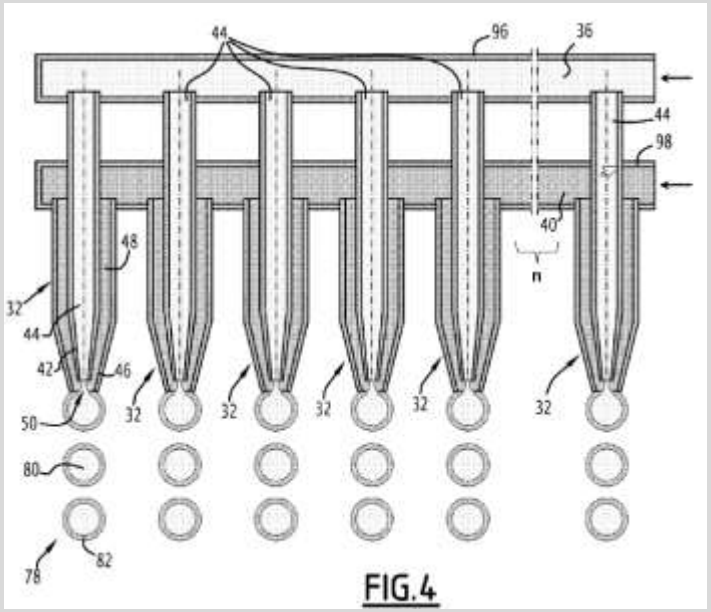
Microencapsulation Example: Polymersomes: Complex Uniform Capsules Drop-by-Drop



Shum, Kim and Weitz, J. Am. Chem. Soc. 2008, *130, 9543–9549*



http://weitzlab.seas.harvard.edu/research/adams-laura.html



capsum design de matière pure

www.capsum.eu

NeoShell™
Beautiful polymersome

Hydrophilic actives
Copolymer di-block bio compatible

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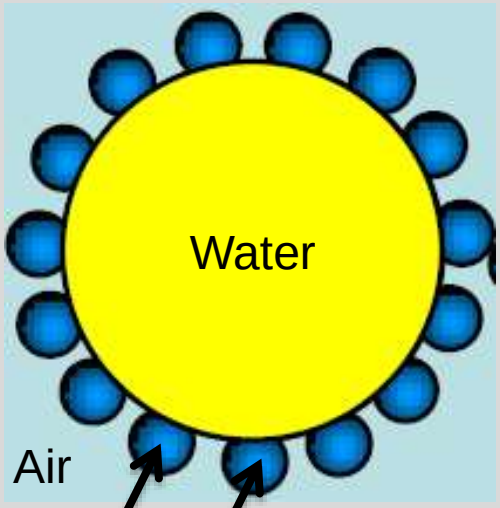
Micro- to Macroencapsulation Example: “Dry Water” - Particles Stabilising Droplets



Hydrophobic silica particles

Prof. Bernie Binks, Univ. Hull

http://scg-hull.theory-sfb569.org/impact-of-our-research/

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Conclusion

- Other industries and applications may be facing the same challenge as you
- Understand their challenges and look at their approaches and solutions
- Formulation has a “universal language”
  - Colloids, particles, dispersions, emulsions, encapsulation…
  - …and the manufacturing technologies too
- Adapt and perfect…

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Thank You!

Forthcoming Courses:

Solid State Stability of Formulations: *The Underlying Science and New Approaches For Rapid Determination*
One-Day Training Course, UK - Nottingham/East Midlands – May 8th 2013

iFormulate*4Nano*: Formulating Nanoparticles
One-Day Training Course, UK- Manchester – June 18th - in collaboration with the NanoFormulation2013 Conference

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