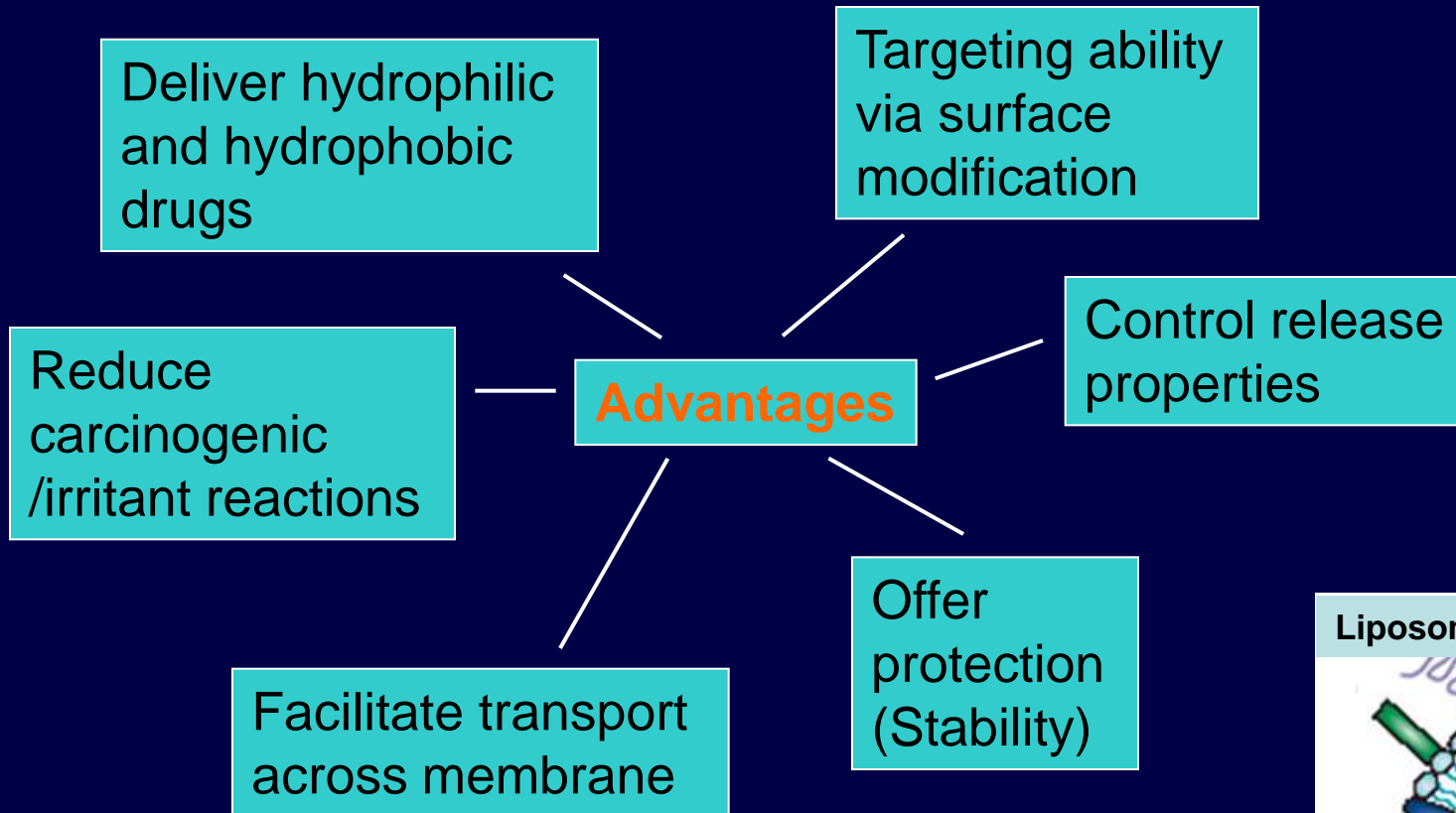


Nanoparticles as Drug Delivery Carriers

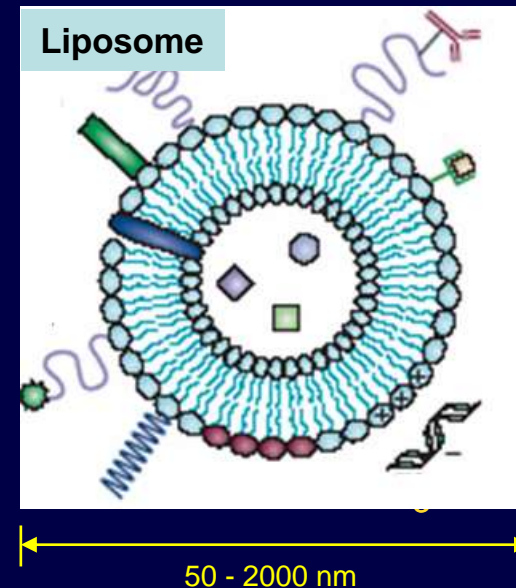
Outline of Presentation :

1. Advantages and Stages of Nanoparticle Delivery Systems
2. Fabrications and **Characterizations** of Nanoparticles
3. Cytotoxicity and Biodistribution of Nanoparticles
4. Interactions between Nanoparticles and Cell membrane (model)
5. Nanotechnology and Cosmetics

Advantages of Nanoparticles - By Convention



Schematic Structure of Liposome Loading with Drug



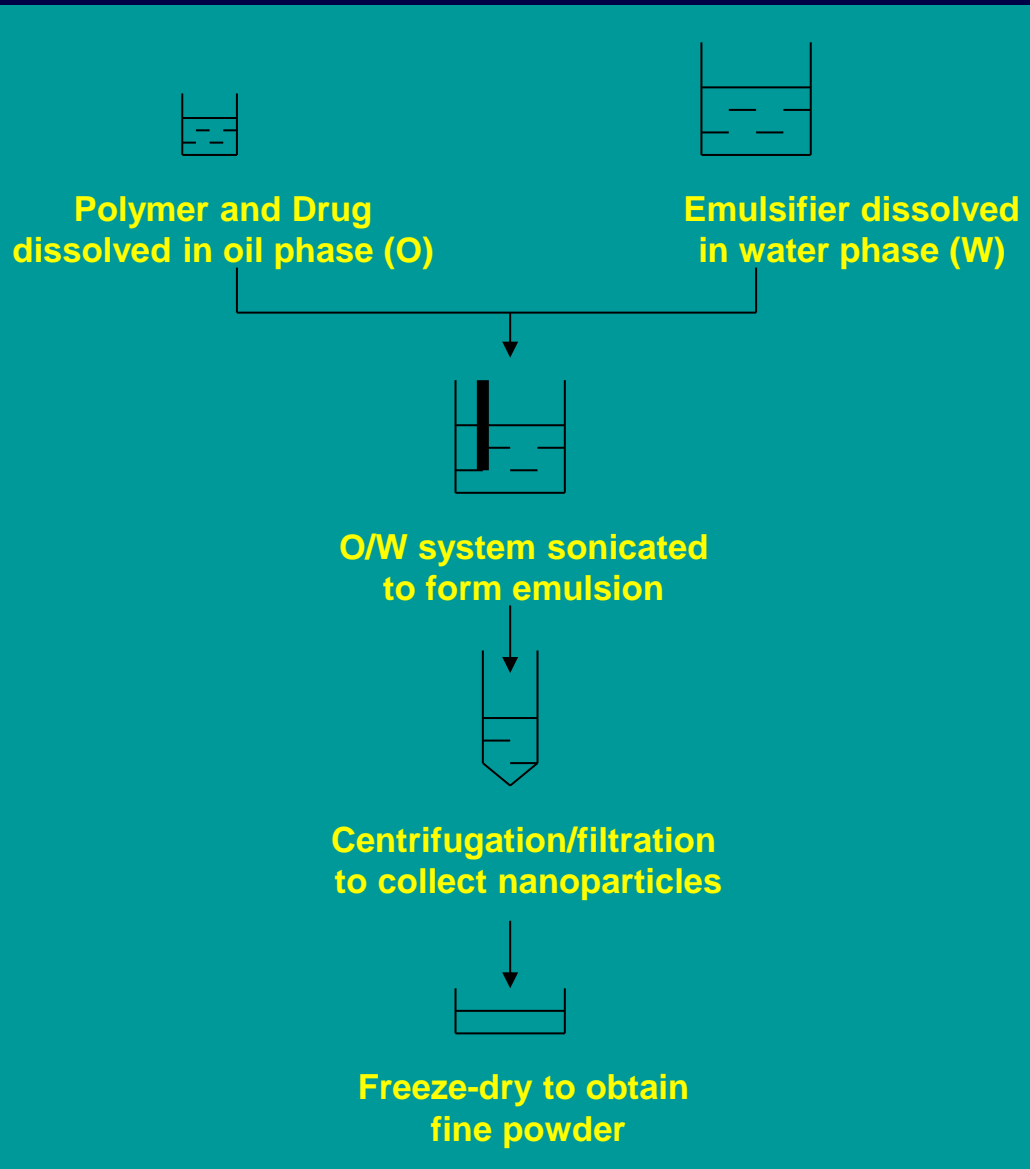
Stages for Developing Nanoparticle Delivery Systems :

1. Materials studies
2. Fabrications
3. **Characterizations** (various analytical methods)
4. Interactions between drug or nanoparticles and cell membrane
5. *In vitro* cytotoxicity (cell viability)
6. Animal tests
7. Clinical trials
8. Commercialisation

Fabrication of Nanoparticles:

- Modified Solvent Extraction/Evaporation Technique
- Spray Drying & Spray Freeze Drying
- Supercritical Fluid Spraying
- Coacervation
- Polymerisation of Monomers
- High-Pressure Hot or Cold Homogenization Process
- Hydration and Extrusion of Lipids or Lipid-polymer Conjugates

Preparation of Polymeric Nanoparticles by Single emulsion solvent extraction/evaporation



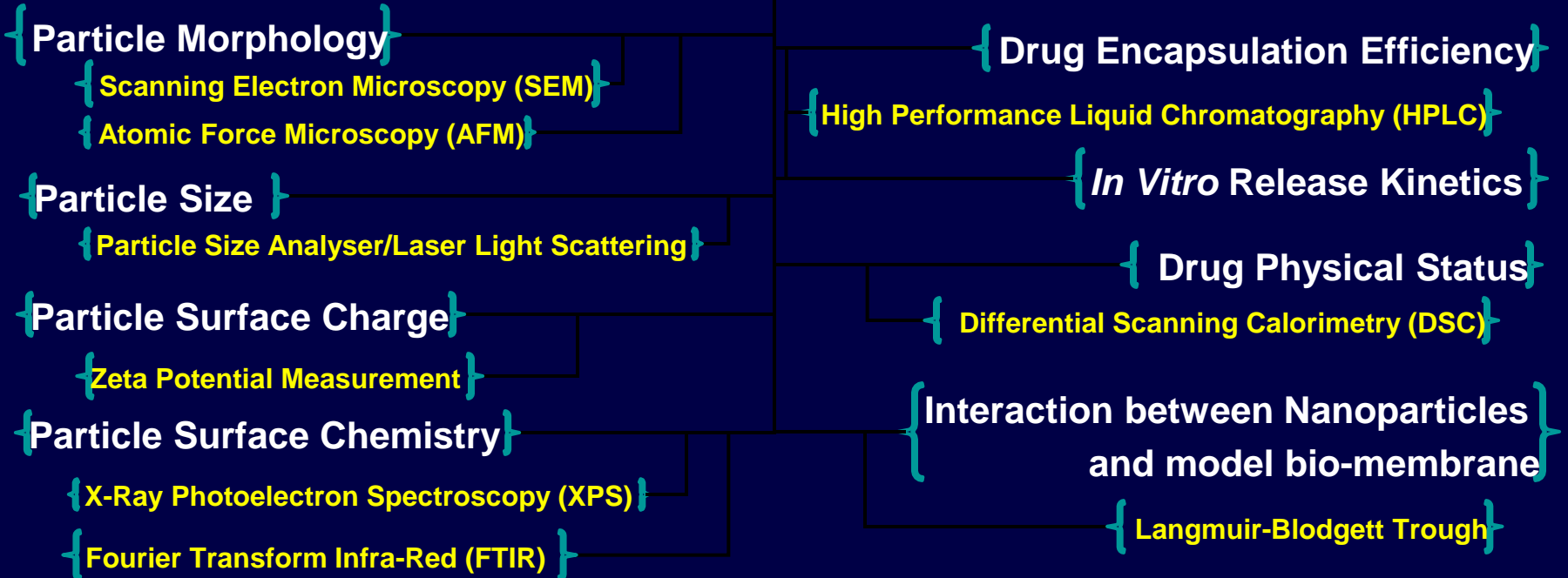
Important parameters:

- Polymer type, MW. and co-polymer blend ratio
- Polymer concentration in oil phase
- Emulsifier/Stabilizer/Additive
- Volume ratio between oil phase (O) and water phase (W)
- Property of organic solvent
- Drug loading proportion to polymeric material
- Mechanical type and strength of mixing
- Drying technique
- Temperature, pH, container, etc.

Methodology

Fabrication

Characterization



In Vitro Cytotoxicity (Cell Viability)

MTS & SRB Assay
ELISA Plate Reader

Animal Experiment

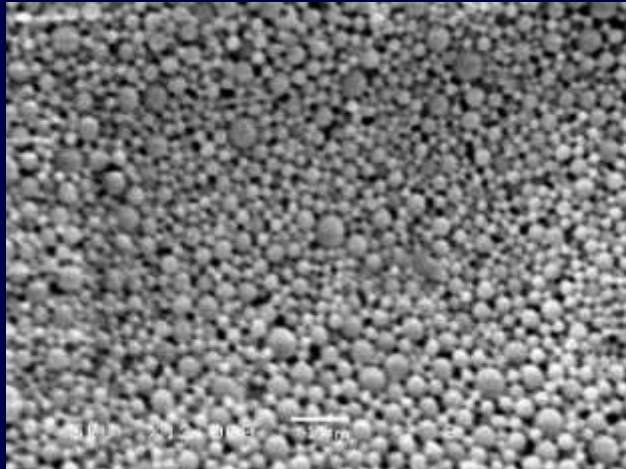
Biodistribution

Maximum Tolerable Doses (MTD)

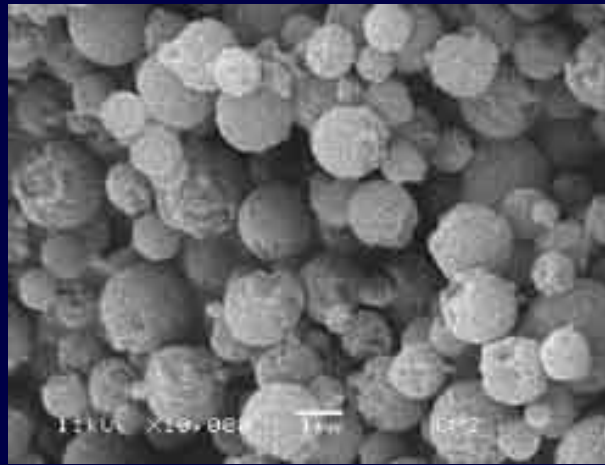
Antitumor Efficacy

Morphology of Drug-loaded Polymeric Nanoparticles

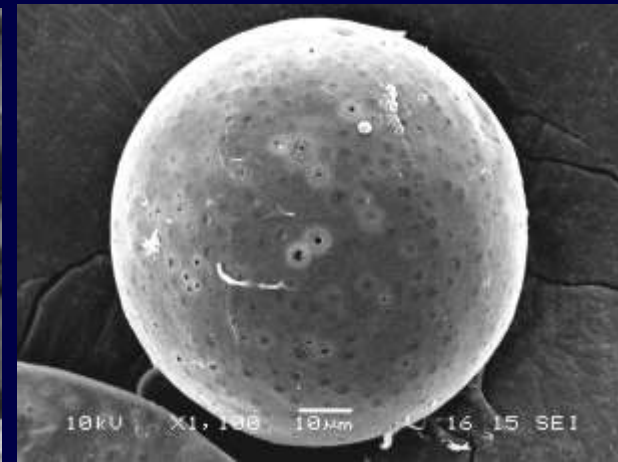
Scanning Electron Microscopy & Atomic Force Microscopy



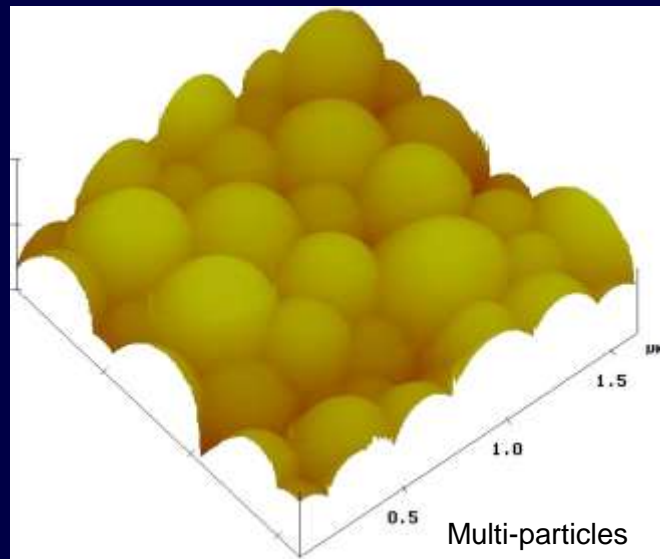
PLGA nanoparticles loaded with Paclitaxel prepared by single emulsification method



PLGA microparticles containing various additives and prepared by spray-drying

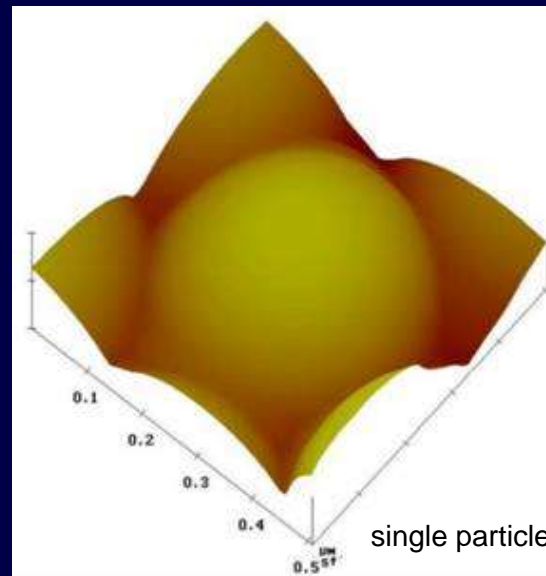


PLGA microparticles prepared by double emulsification method

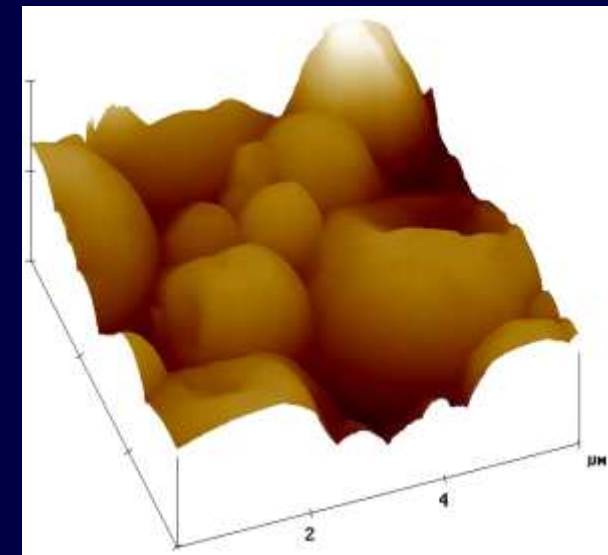


Multi-particles

PLGA-TPGS nanoparticles prepared by single emulsification

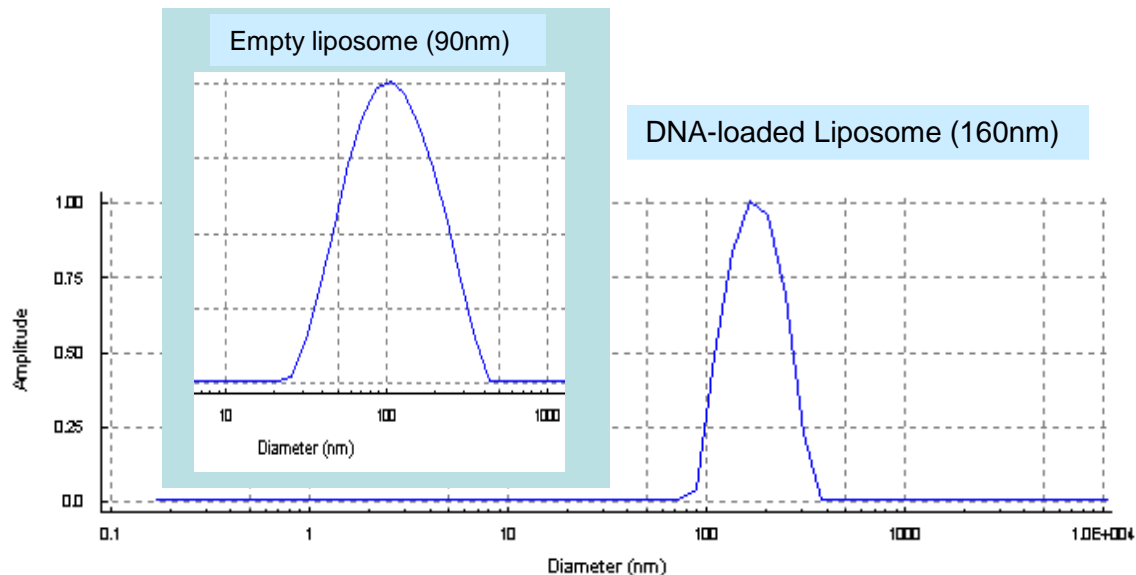
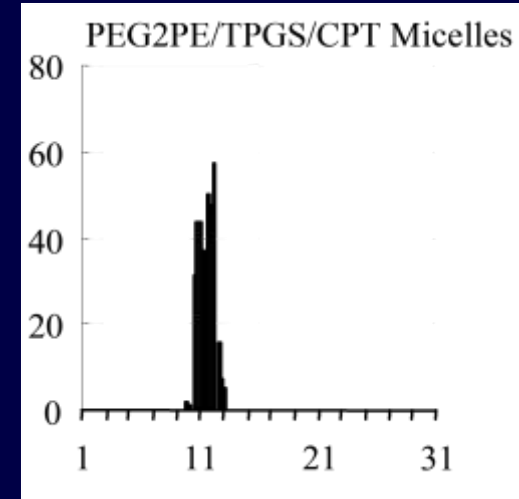
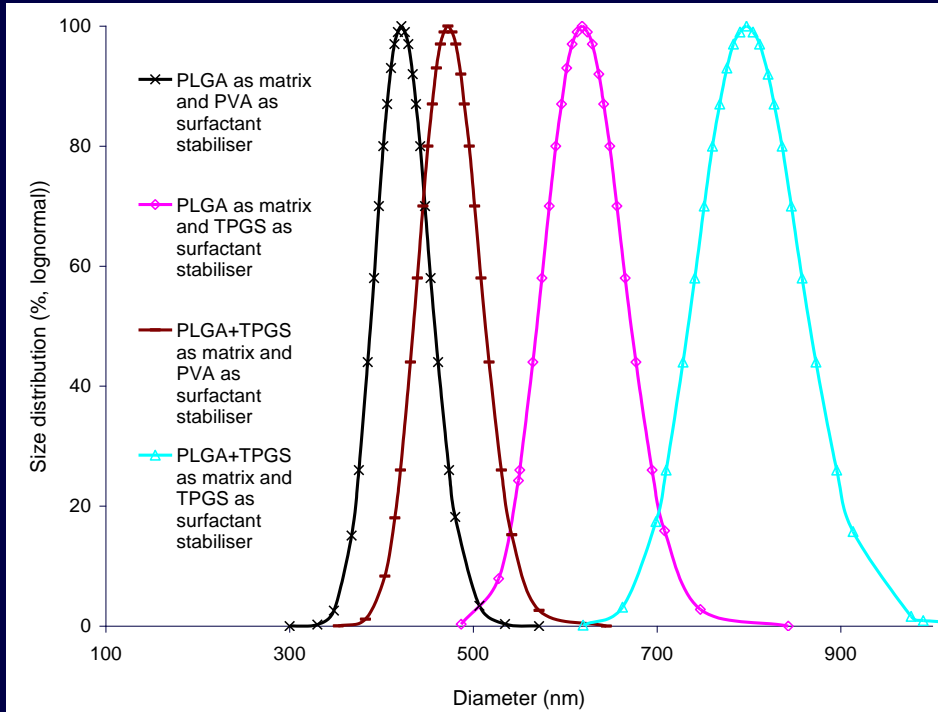


single particle

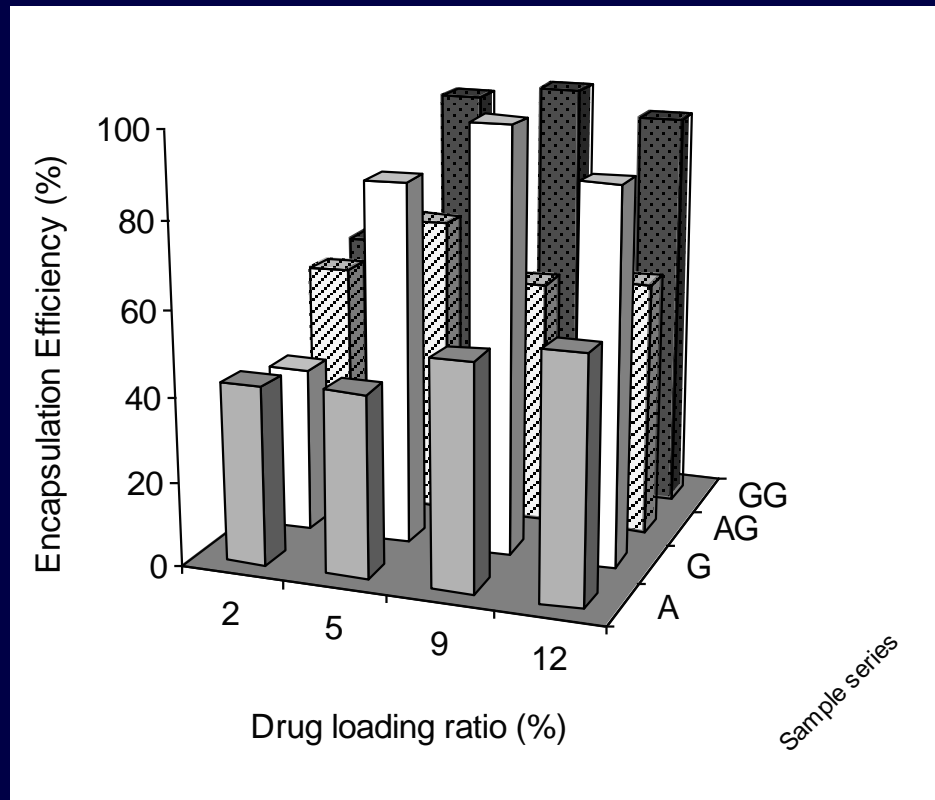


PLGA-TPGS microparticles prepared by spray-drying technique

Particle Size and Size Distribution



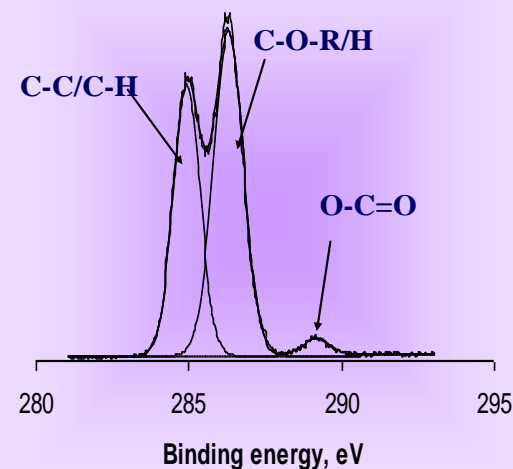
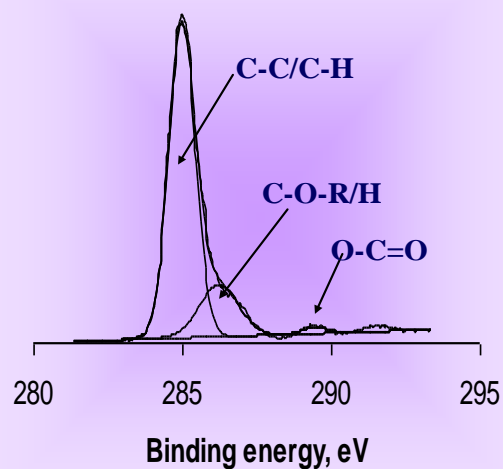
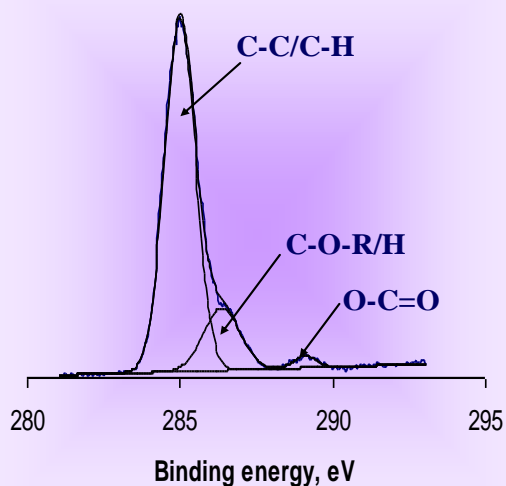
Drug Encapsulation Efficiency



Paclitaxel encapsulation efficiency of various nanoparticulate formulations (Nanoparticles prepared with TPGS as surfactant stabilizer (G and GG series) exhibited higher drug EE compared with those prepared with PVA as emulsifier (A and AG series))

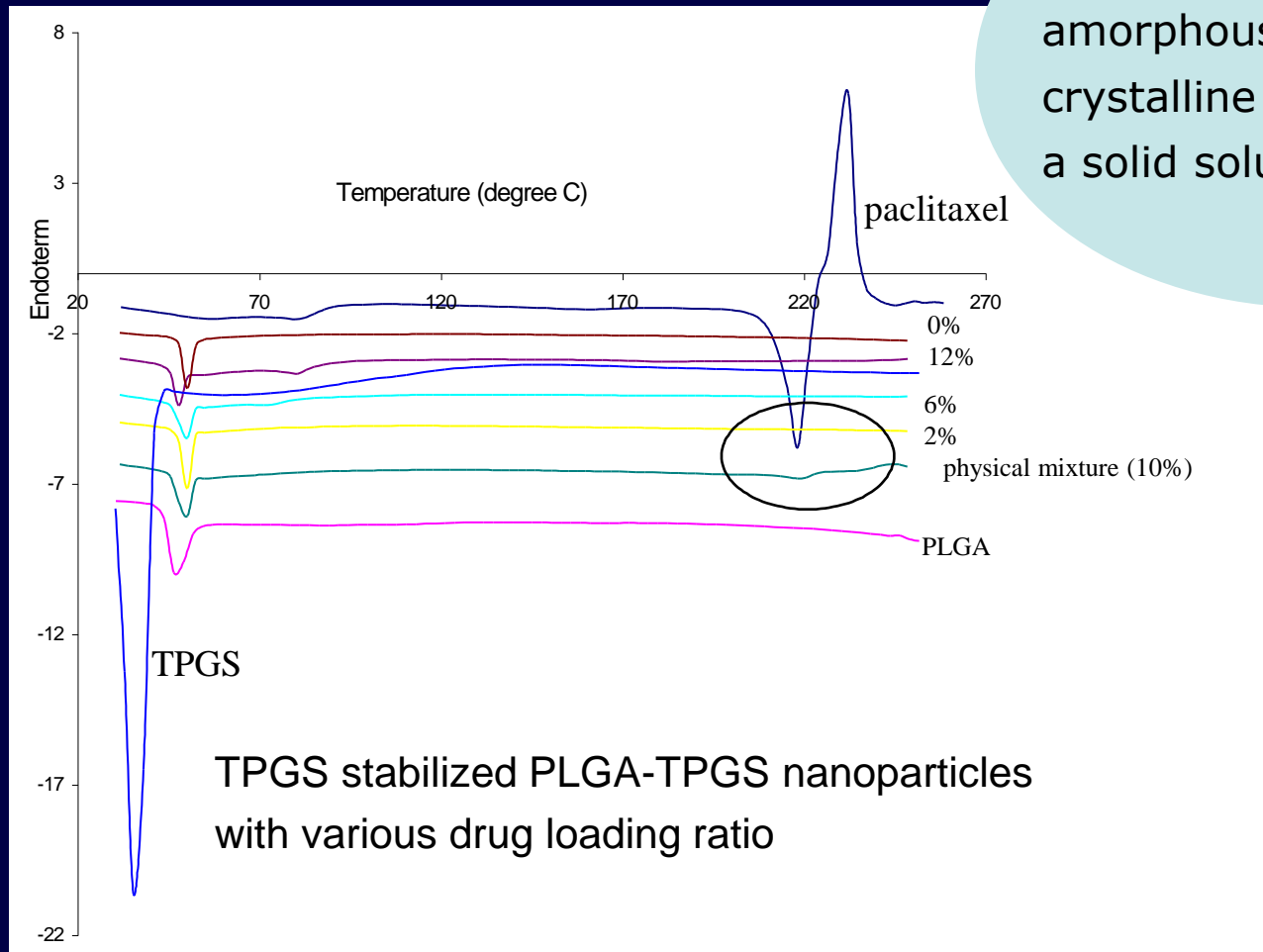
X-ray Photoelectron Spectroscopy Analysis of Particle Surface

Samples	XPS C1s envelope ratio (%)		
	C-C/C-H	C-O-H/C-O-R	O-C=O
Uncoated Polystyrene particles	81.24	16.85	1.91
Pure TPGS	84.77	13.73	1.50
TPGS-coated particles	84.33	12.32	3.35
Pure PVA	48.91	42.55	8.54
PVA-coated particles	41.84	55.52	2.64



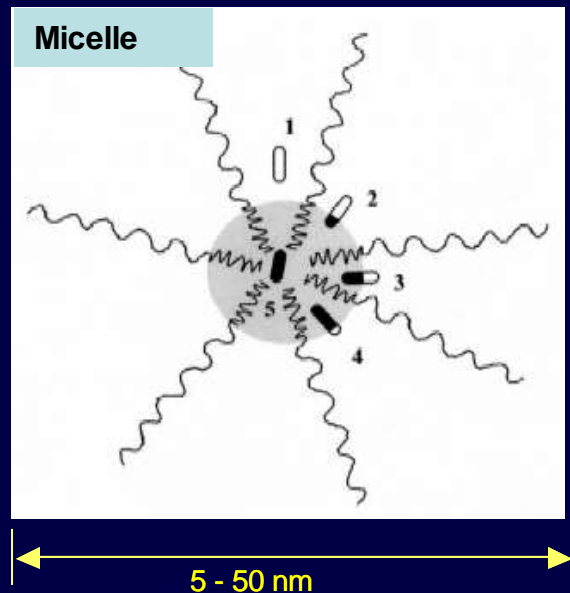
Thermal Analysis & Drug Physical Status

Differential Scanning Calorimetry (Paclitaxel Encapsulated in Polymeric Nanoparticles)

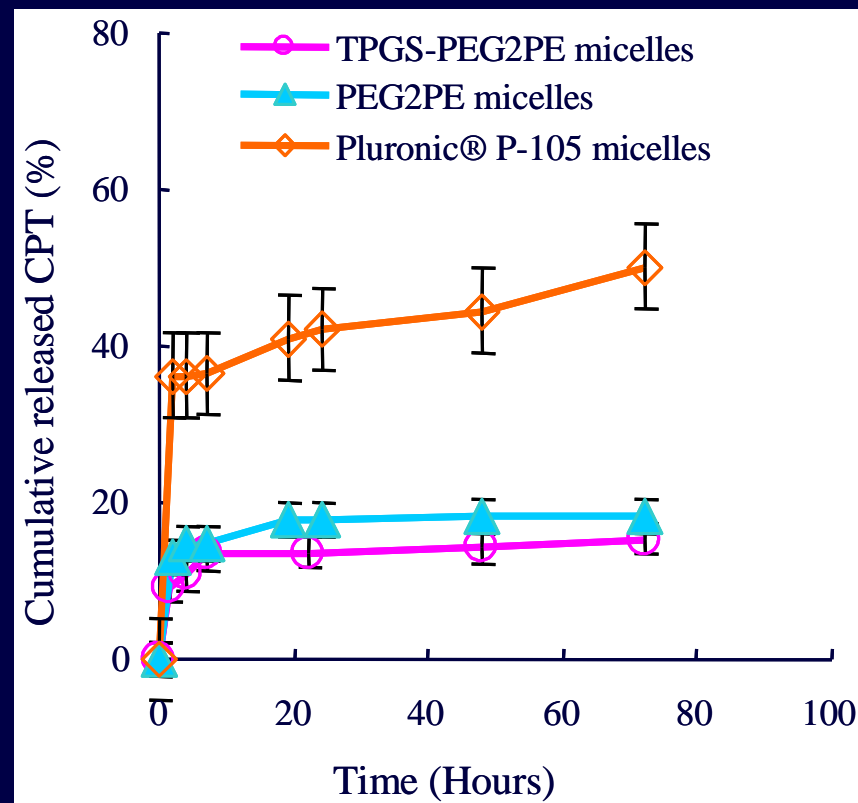


Drug entrapped was in an amorphous, or disordered-crystalline phase state, or a solid solution state

In Vitro Release Property



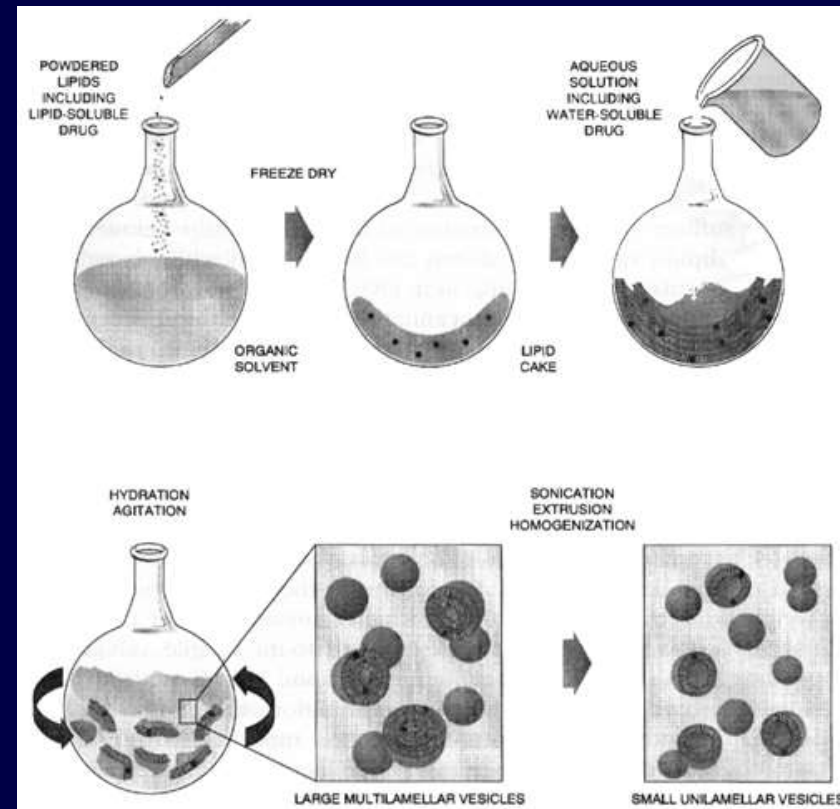
Micellar nanoparticle from lipid-polymeric conjugate is good carrier for water insoluble drug.



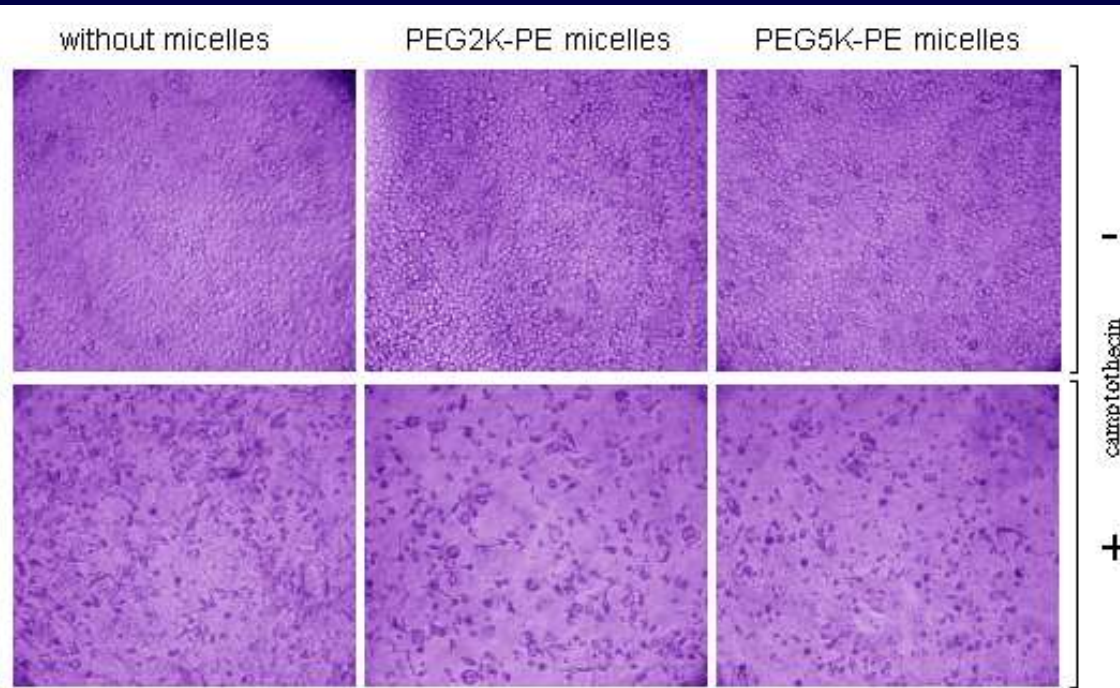
In vitro release of camptothecin from various micelle formulations

Special attention to liposome delivery formulations for protein/DNA (Issues/Challenges):

- Dosage variability (Possible over- or under-dosing of the recipient):
 - Special training of personnel
 - Preparation of the complex by admixture prior to each use
- Inconvenient for large scale production
- Purification
- Different effects in different cells types
- Storage/formulation stability (Forming large and less active aggregates)
- Lyophilization



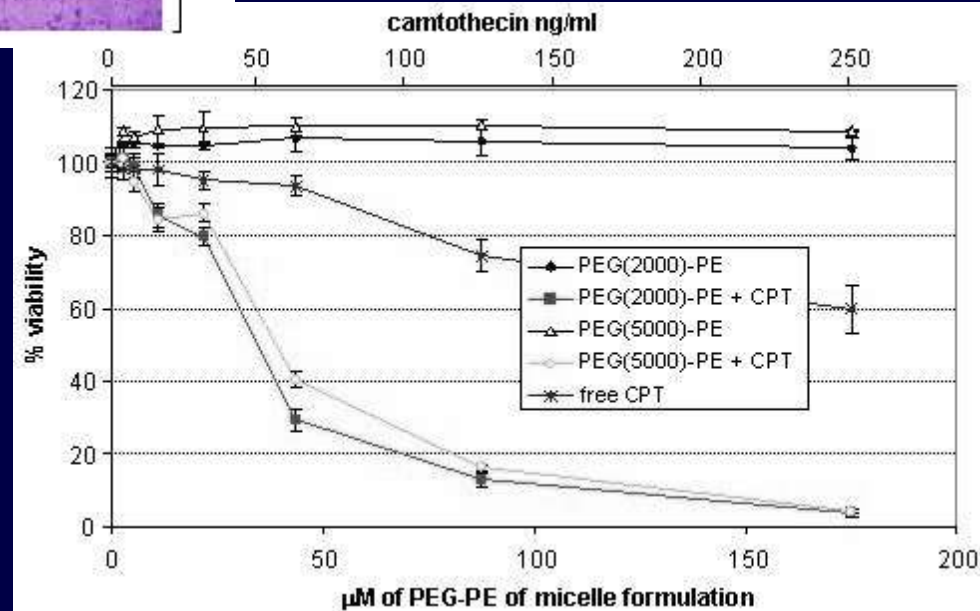
Cell Cultures & Cytotoxicity Assays



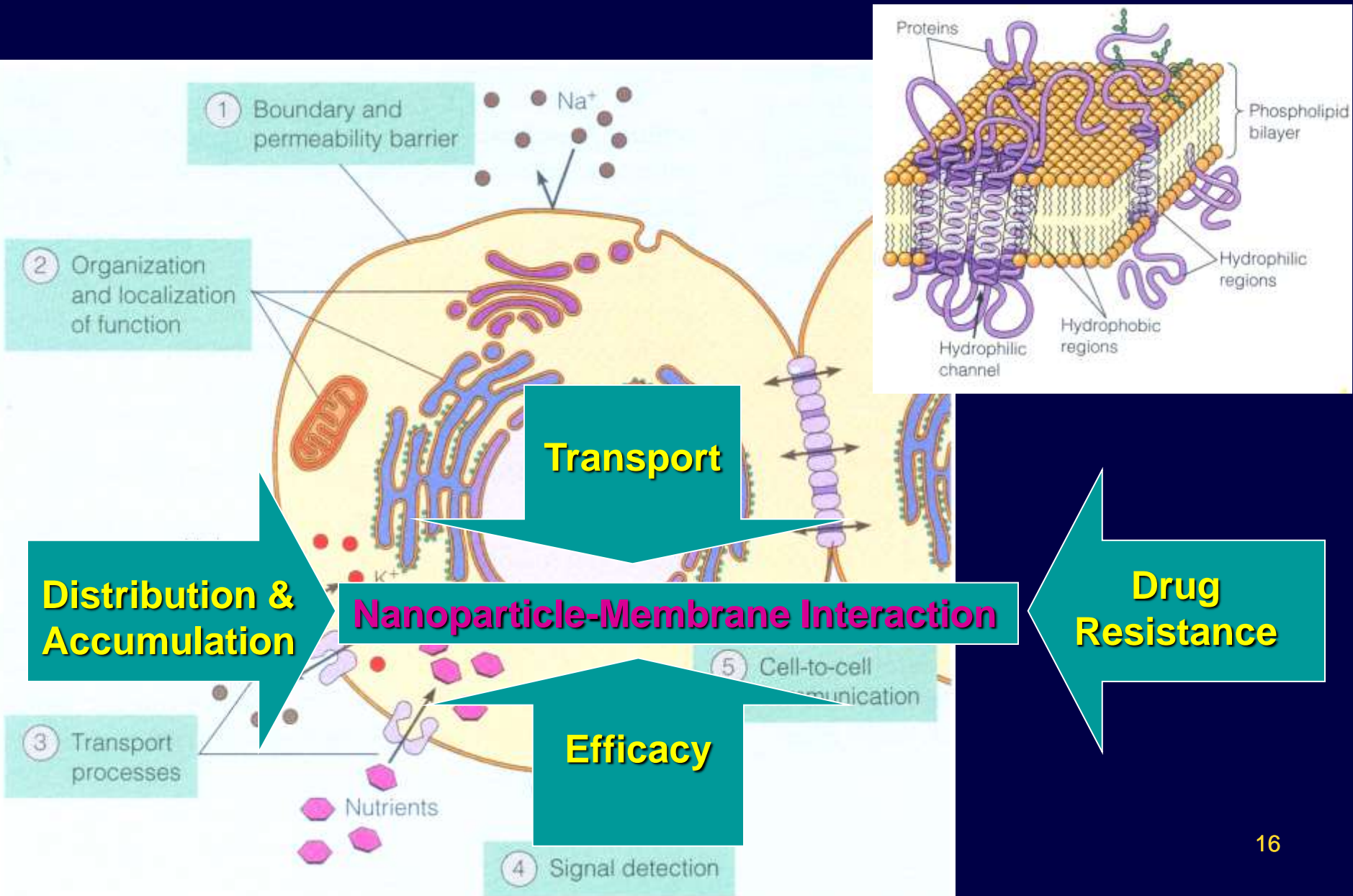
Cell morphology and cytotoxicity of free CPT and CPT-loaded PEG-PE micelles in HT-29 cell Culture. (Picture was taken at CPT conc. about 130 ng/ml)

Reason of enhanced cytotoxicity of the micellar drug:

- Increased solubility of the poorly soluble drug in micelle solution;
- Increased stability of the drug molecule inside the micelle core;
- Better uptake of drug-containing micelle nanoparticles by the cells.

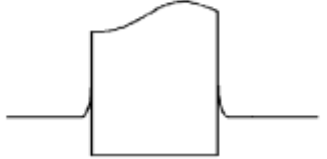


Interactions Between Nanoparticles and Model Membrane

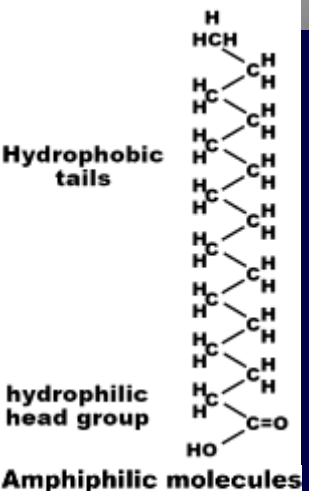


Langmuir Trough for Monolayer Study

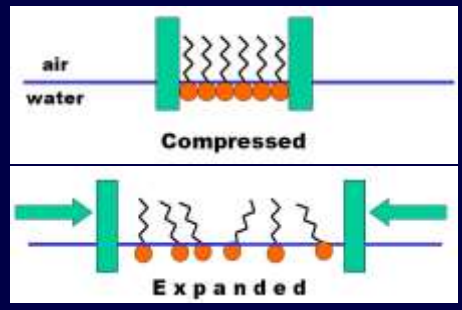
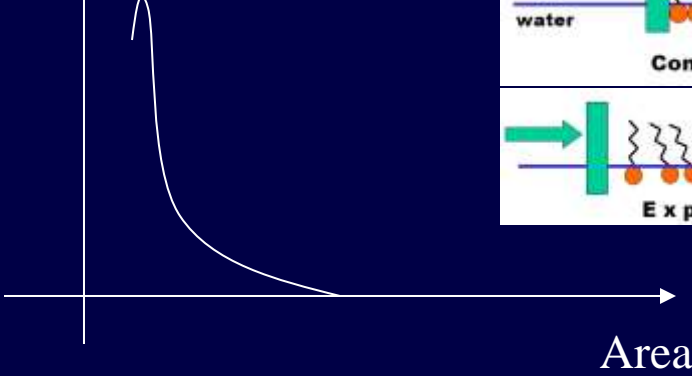
Surface pressure measurement
The Wilhelmy Plate



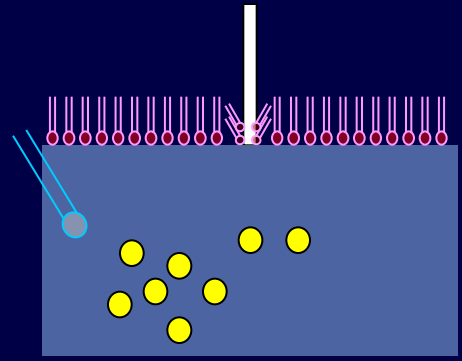
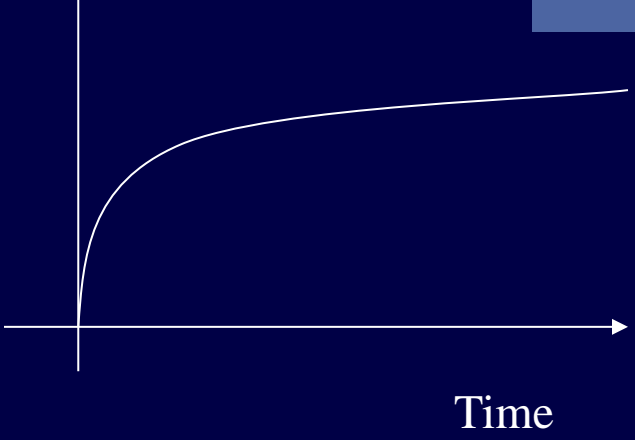
Force = weight - upthrust + surface tension



Surface Pressure, Π (mN/m)

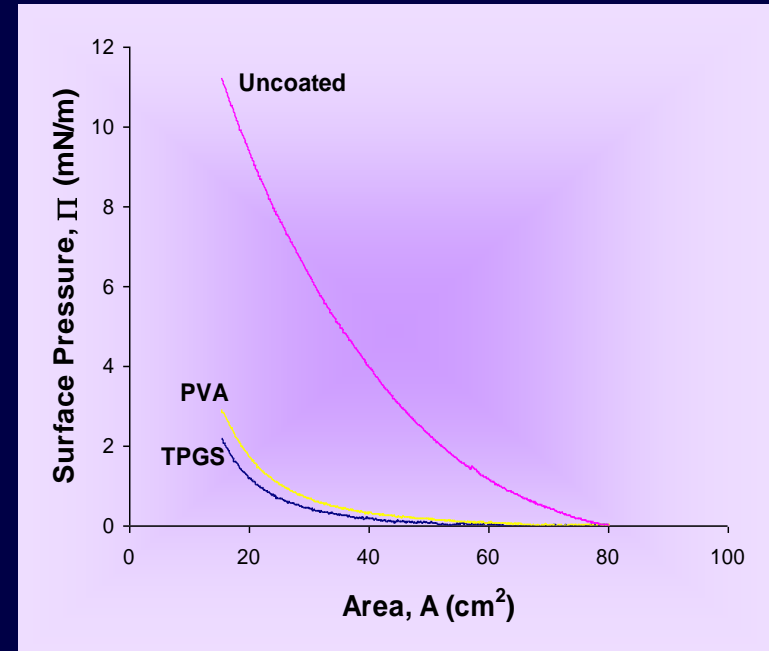
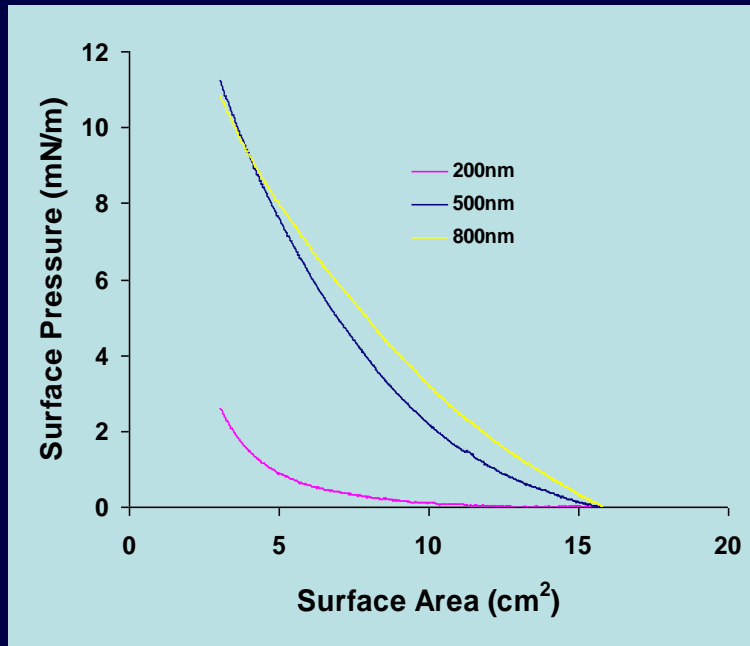


$\Delta\Pi$ (mN/m)



Time

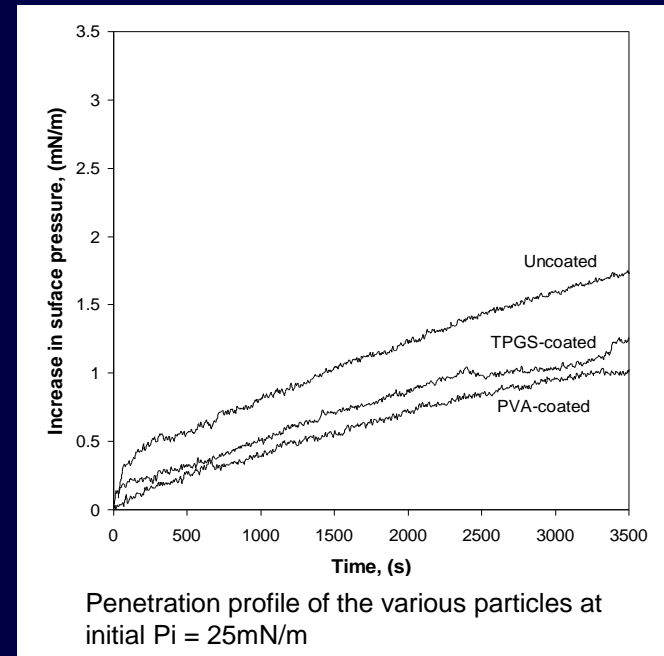
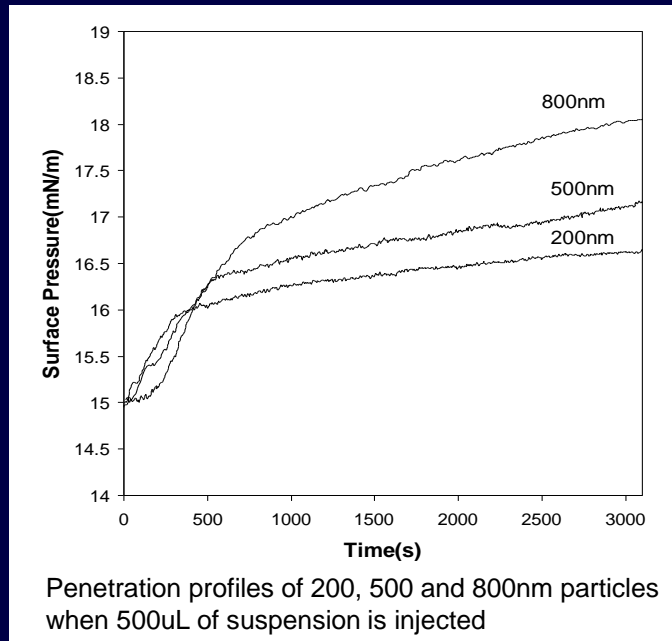
Inter-particle Forces and Pi-A Isotherms



Surface pressure Π is a function of following interfacial forces

Kinetic & Van der Waals & Capillary & Electrostatic charge repulsion

Particle-Membrane Interaction and Penetration



The particle penetration process may involve:

- **Diffusion** of particles to the monolayer interface
- **Insertion** of the particles into the monolayer
- **Rearrangement** of the adsorbed particles at the interface

1 Medicine

- 1.1 Diagnostics
- 1.2 Drug delivery
- 1.3 Tissue engineering

2 Chemistry and environment

- 2.1 Catalysis
- 2.2 Filtration

3 Energy

- 3.1 Reduction of energy consumption
- 3.2 Increasing the efficiency of energy production
- 3.3 The use of more environmentally friendly energy systems
- 3.4 Recycling of batteries

4 Information and communication

- 4.1 Memory Storage
- 4.2 Novel semiconductor devices
- 4.3 Novel optoelectronic devices
- 4.4 Displays
- 4.5 Quantum computers

5 Heavy Industry

- 5.1 Aerospace
- 5.2 Refineries
- 5.3 Vehicle manufacturers

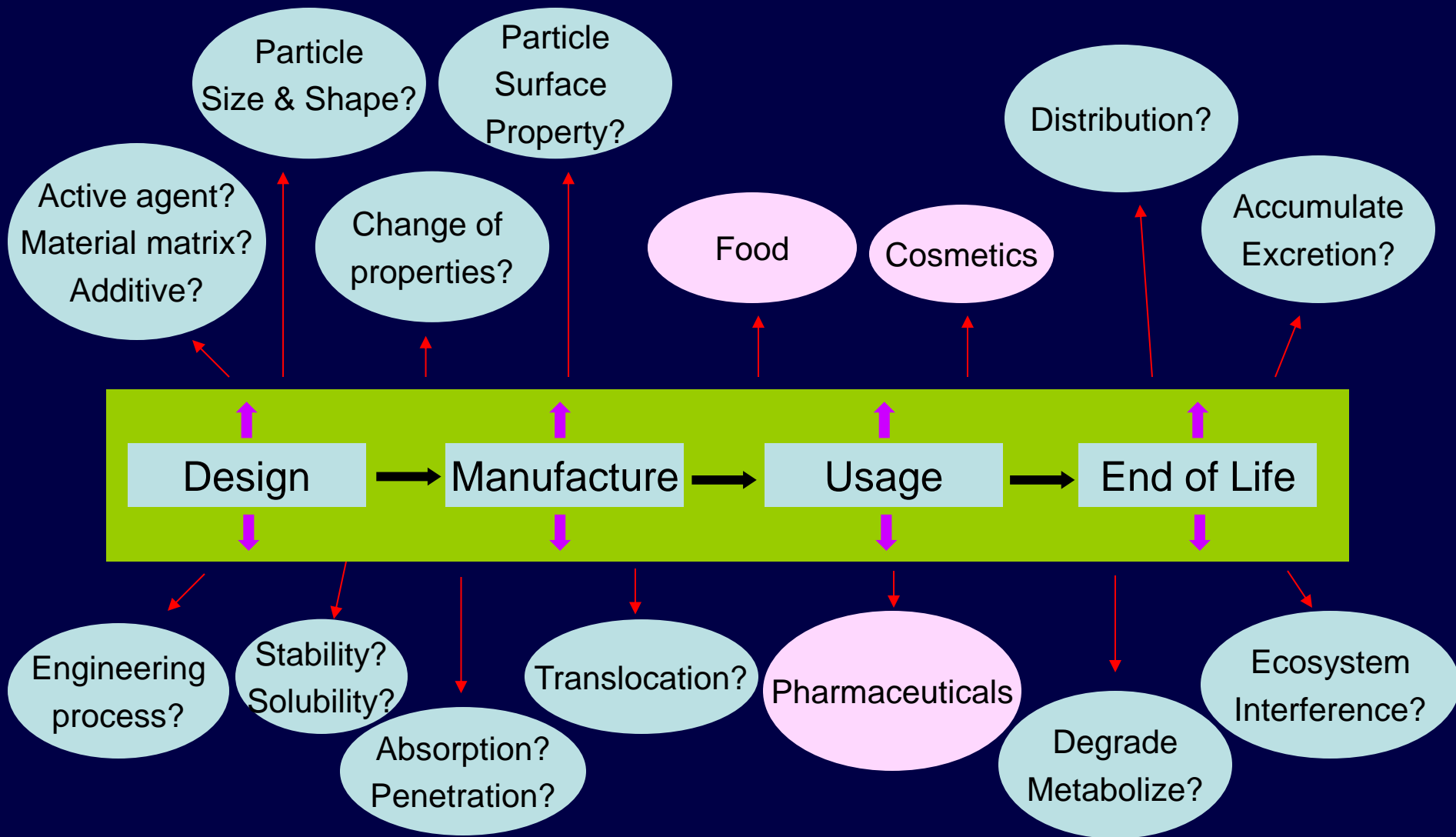
6 Consumer goods

- 6.1 Foods
- 6.2 Household
- 6.3 Optics
- 6.4 Textiles
- 6.5 Cosmetics

7 References

**Bioavailability
Toxicity!**

Environmental Impacts and Health Effects



Thank you for your attention!