



# Nanoscale Materials in Medicine

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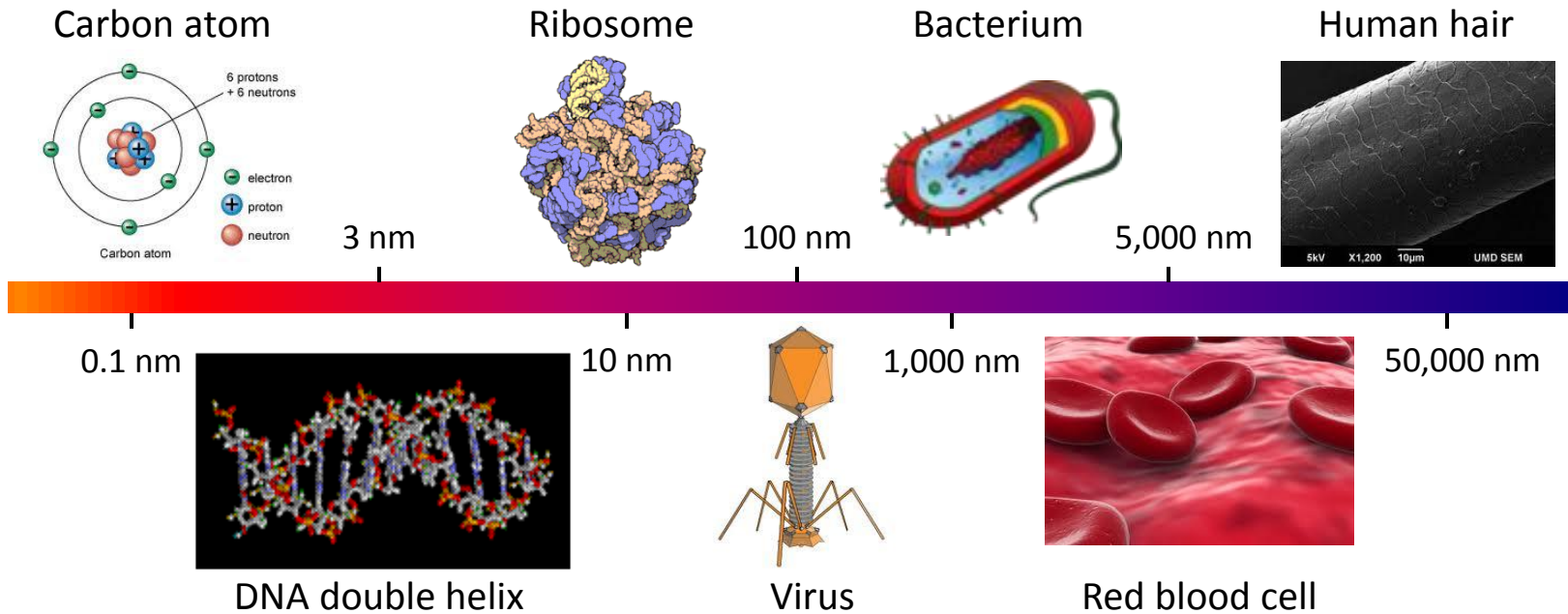
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# Nanoscale Materials in Medicine

Nanoscale materials are the ideal size to therapeutically interact with and selectively influence cellular entities and processes at their natural scale.

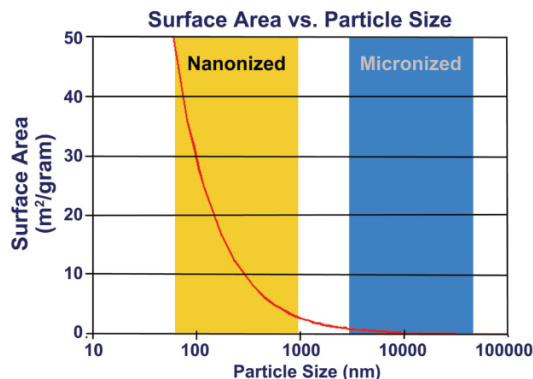


Nanoscale materials have been used for:

- Targeted drug delivery
- Controlled drug release
- Dissolution rate enhancement
- Molecular diagnostics
- Contrast enhancement in imaging
- Gene therapy

# Size Dependent Properties of Nanoparticles

## Surface Area (per unit mass)



## Percentage of Surface Molecules

Particle size (nm)	Surface molecules (%)
1	100.00
10	27.10
100	2.97
1,000	0.30

## Dissolution Rate

Noyes-Whitney Equation

$$\text{Dissolution Rate} = \frac{A \cdot D}{h} (C_s - C_b)$$

A = surface area

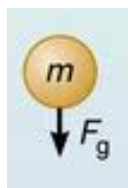
D = diffusivity

h = boundary layer thickness

C<sub>s</sub> = saturation solubility

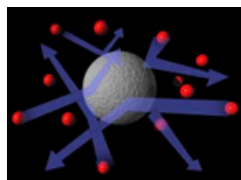
C<sub>b</sub> = bulk concentration

## Settling Velocity and Brownian Motion



Settling Velocity

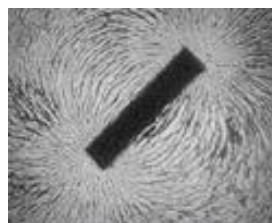
$$v = \frac{d^2 g (\rho_s - \rho_l)}{18 \mu_l}$$



Brownian Displacement

$$x = \sqrt{\frac{2k_B T t}{\pi \mu d}}$$

## Magnetic Properties



Ferromagnetic materials become superparamagnetic below ~20 nm

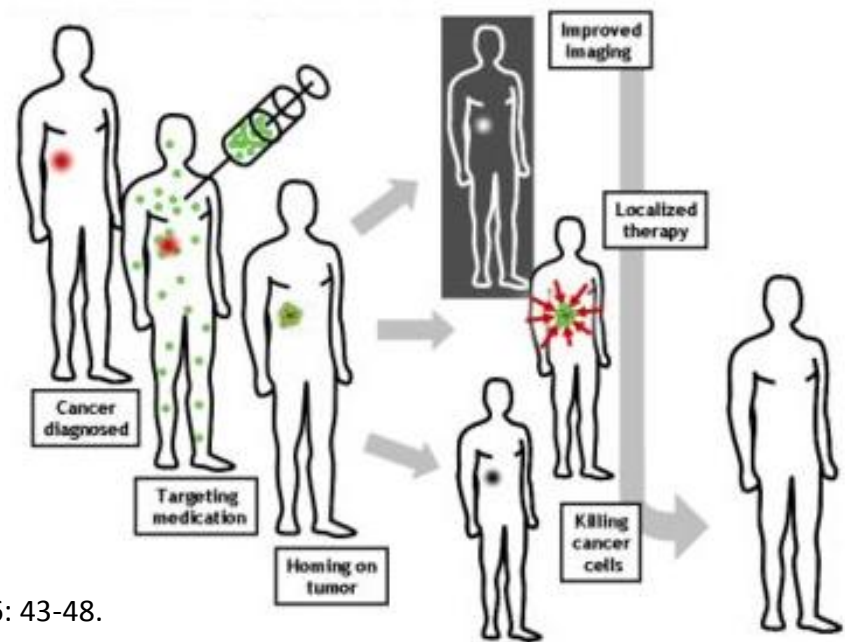
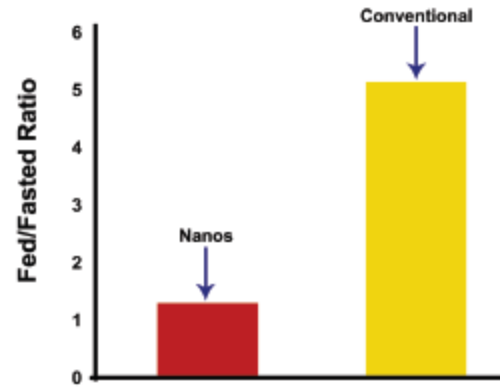
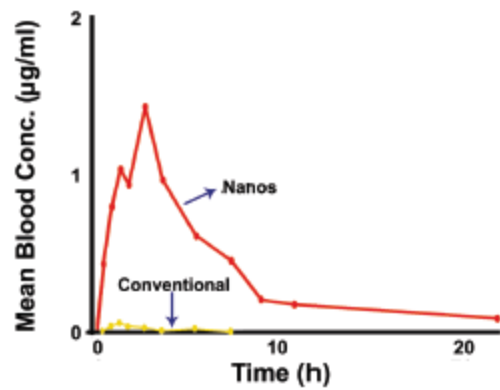
## Optical Properties



Size dependent fluorescent emission colors of ZnS-capped CdSe nanoparticles under UV light

# Advantages of Nanoparticles in Medicine

- Nanoparticles dissolve faster, and thus possess increased potency, due to their increased surface area
- Nanoparticles are less effected by the fed/fasted state, delivering more consistent performance
- Nanoparticles can enhance imaging contrast, allowing for more accurate diagnostics
- Nanoparticles can be delivered directly to an effected site, minimizing side effects

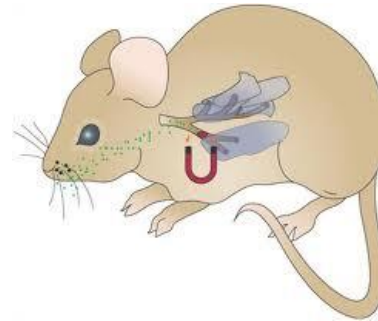


# Efficient Delivery of Therapeutic Nanoparticles

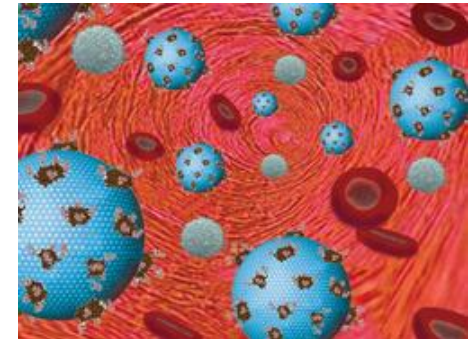


Routes and delivery systems by which therapeutic nanoparticles can be delivered:

- Peroral
  - Nanoparticulate suspensions
  - Tablets
- Parenteral
  - Nanoparticulate suspensions
  - Implants
- Pulmonary
  - Aerosol suspensions
  - Dry powder inhalers
- Ocular
  - Ocular inserts
  - Mucoadhesive gels
- Topical
  - Ointments
  - Transdermal patches



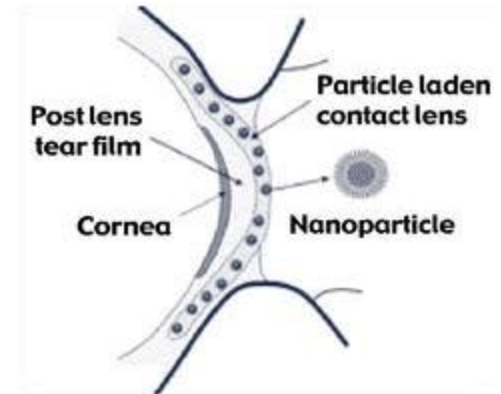
**Localized delivery of magnetic nanoparticles**



**Inhaled nanoparticles in the brain**



**Injectable gel of therapeutic nanoparticles**



**Drug delivery from a soft contact lens**

Date, A. A. and V. B. Patravale. 2004. *Current Opinion in Colloid & Interface Science* 9(3-4): 222-235.

National Institute of Advanced Industrial Science and Technology.

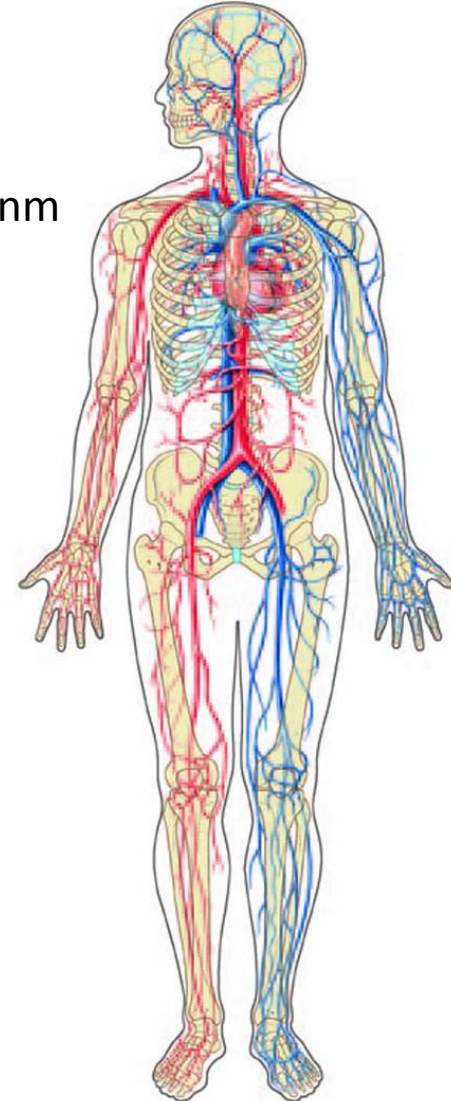
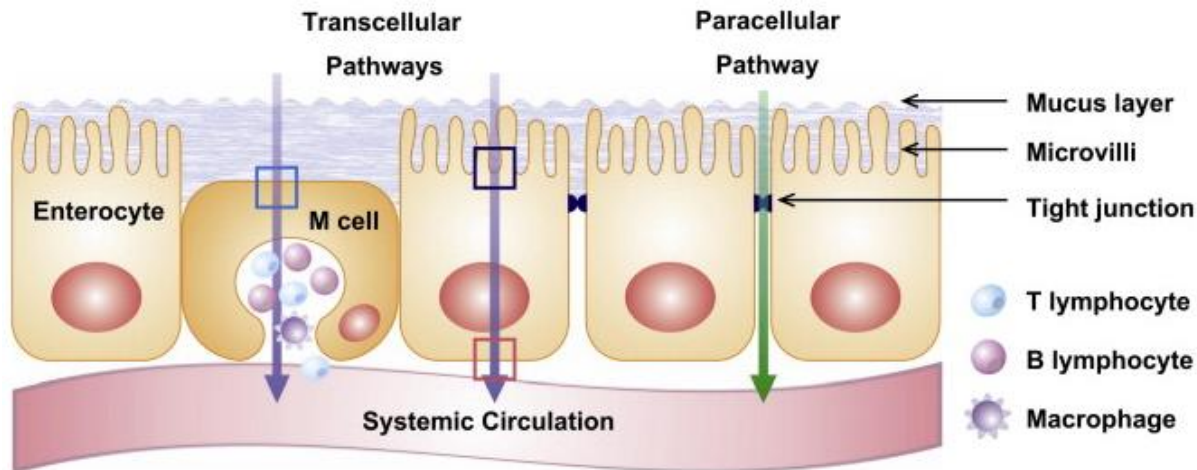
Jha, G. and A. Kumar. 2011. *Chronicles of Young Scientists* 2(1): 3-6.

# Biological Transport of Nanoparticles



- Nanoparticles typically reach their targeted site through circulatory transport or through tiny openings at cellular or subcellular membranes.
- The diameter of the narrowest capillaries is approximately 2000 nm
- For efficient transport, nanoparticles should be < 300 nm
- Transport across membranes can be transcellular or paracellular

## Uptake of Nanoparticles in the Intestinal Epithelium

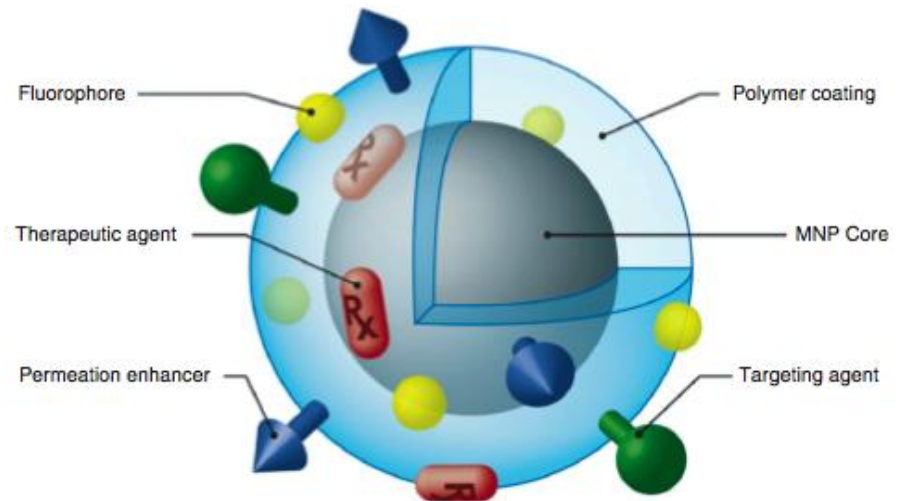


# Modified Nanoparticles for Multifunctionality



• Nanoparticles can be modified by coatings and surface ligands to:

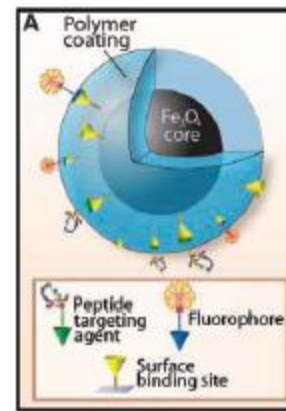
- Prevent nanoparticle aggregation
- Selectively accumulate in tumor tissue
- Deliver therapeutics
- Avoid macrophage uptake
- Extend circulation time
- Enhance contrast for imaging



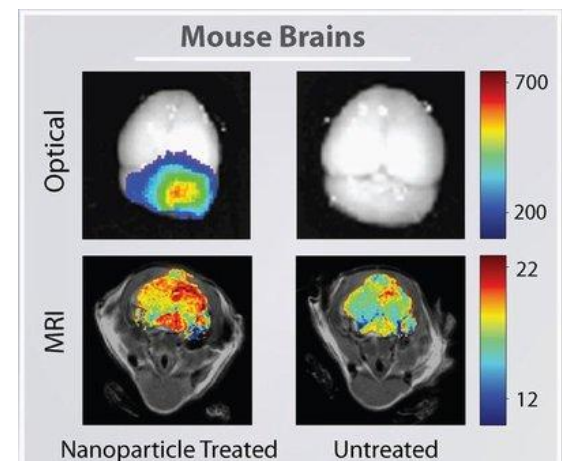
**Generic multifunctional nanoparticle**

• Enhanced imaging contrast was achieved in mice brain tumors using functionalized iron oxide nanoparticles

- PEGylated chitosan–branched copolymer coating
- Chlorotoxin targeting ligand
- Near-IR fluorophore

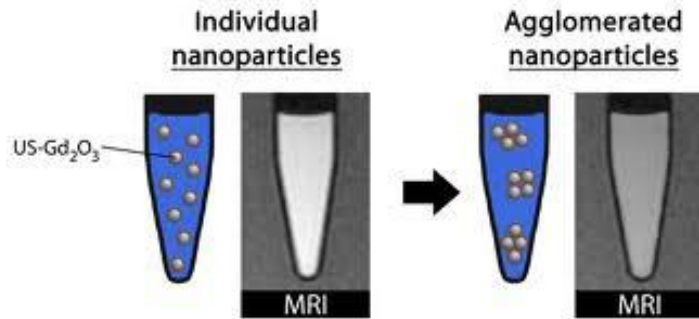


**Imaging of mouse brain tumors**

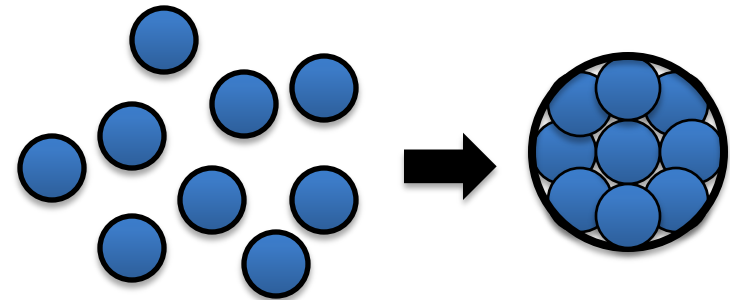


# Challenges in Nanoparticle Formulation

- The high surface energy of nanoparticles causes them to agglomerate, losing their unique size dependent properties.



Lack of contrast from agglomerated nanoparticles



Loss of surface area from agglomeration

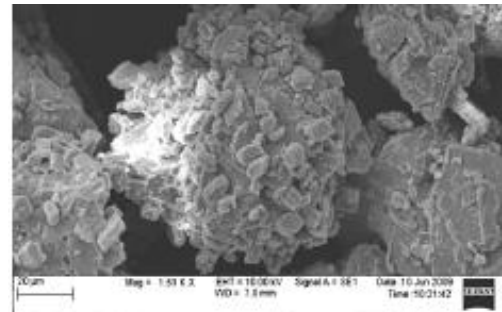
- There are still many questions regarding the use of therapeutic nanoparticles
  - Ability of nanoparticles to penetrate the blood-brain barrier could be problematic
  - Potency of nanoparticle formulations could increase undesirable side effects
  - Nanoparticles could cause side effects not observed with conventional formulations
  - Public perception of nanoparticles is sometimes negative



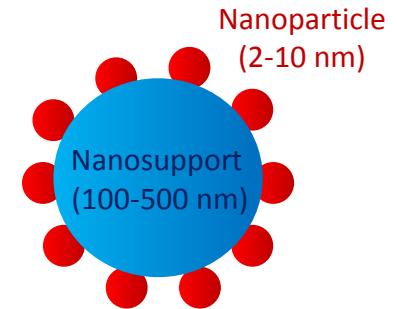
# Unique Nanoparticle-Based Formulations



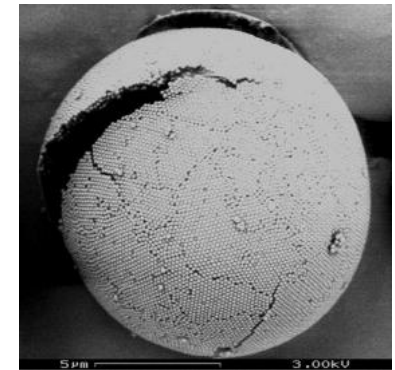
- Nanoparticles can be deagglomerated by precipitation on larger pharmaceutical carriers (e.g. lactose, cellulose, etc.)



Nevirapine particles on the surface of a lactose particle

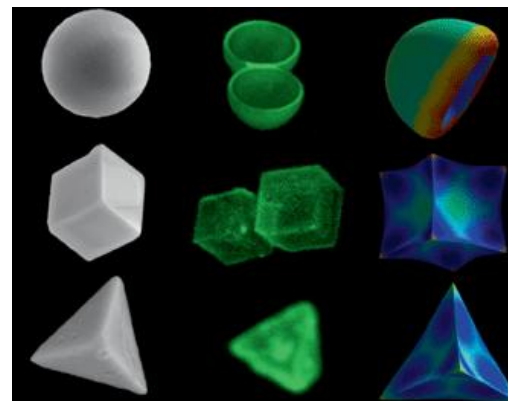


- Porous nanoparticle aggregate particles (PNAPs) have been developed to deliver drugs deep within the lung but prevent nanoparticle expulsion during exhalation

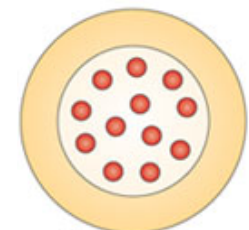


Porous nanoparticle aggregate particle

- Unique nanoparticle morphologies have been examined for their potential in controlled release applications



Anisotropic nanoparticles

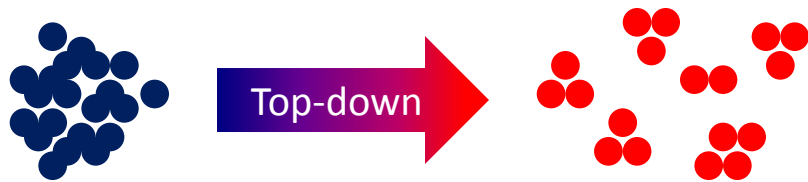


Nanocapsule

# Production of Nanoparticles

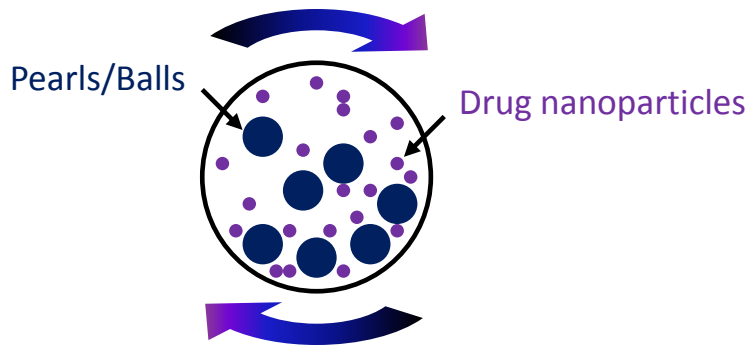
## Top-Down Production

Disassembling macroscale materials into nanoscale constituents through applied force



Examples:

- Pearl/ball milling
- High pressure homogenization



Rotating pearl/ball mill

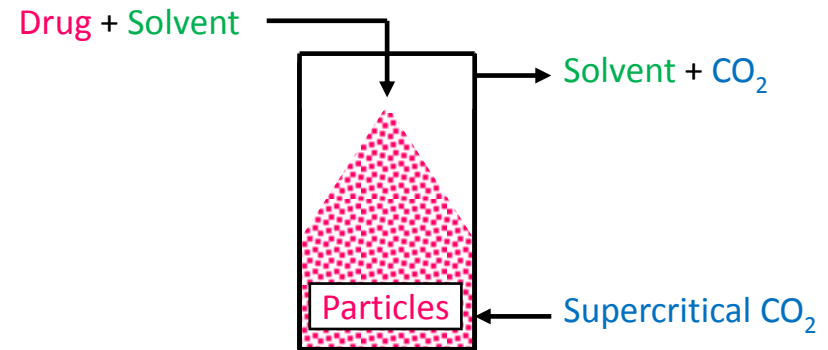
## Bottom-Up Production

Assembling nanoscale materials from molecular solutions through precipitation



Examples:

- Supercritical fluid precipitation
- Emulsification-diffusion



Supercritical antisolvent (SAS) precipitation

# Commercial Nanoparticle Products

- In 2005, the FDA approved Abraxane™, an intravenous formulation of 130 nm paclitaxel loaded albumin nanoparticles
  - Decreased toxicity compared to previous formulations
  - Improved efficacy
- The performance, administration, and storage of numerous drugs have been enhanced through nanoparticle formulations produced by media milling (Nanocrystal® Technology, Elan)

**Abraxane**  
(nanoparticle albumin-bound paclitaxel)

