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Khosro Adibkia

Associate professor

Department of Pharmaceutics

Tabriz University of Medical Sciences

Iran



Honors and awards:

1. Awarded prize for the best educational pattern of Tabriz University of Medical Sciences ,5th Educational Festival of Shahid Motahari, Tabriz, Iran (2013).
2. Awarded prize for the best educational pattern of Tabriz University of Medical Sciences ,4th Educational Festival of Shahid Motahari, Tabriz, Iran (2012).
3. Selected as the distinguished researcher of East Azerbaijan Province, Iran. (2010).
4. Awarded prize for the best PhD student of Tabriz University of Medical Sciences, Tabriz, Iran. (2009)
5. Winner of Rhazes (Razi) Research prize (first rank in novel drug delivery systems) in Iran. (2008)
6. Selected as a Member of the [National Elites Organization](#) (2008).
7. Awarded prize for the best PhD student of Tabriz University of Medical Sciences, Tabriz, Iran. (2008)
8. Awarded prize from the President of Iran for the best PhD student of Iran. (2007)
9. Awarded prize for the best PhD student of Tabriz University of Medical Sciences, Tabriz, Iran. (2007)

Recently published articles

1. Application of electrospraying as a one-step method for the fabrication of triamcinolone acetonide-PLGA nanofibers and nanobeads, *Colloids and Surfaces B: Biointerfaces*, 2014.
2. Antimicrobial Activity of the Metals and Metal Oxide Nanoparticles, *Materials Science and Engineering C*, 2014.
3. In vitro and In vivo evaluation of Clarithromycin-Urea solid dispersions prepared by solvent evaporation, electrospraying and freeze drying methods, *Powder Technology*, 2014.

Principles of Drug Delivery and Pharmaceutical Nano Technology

Drug Delivery

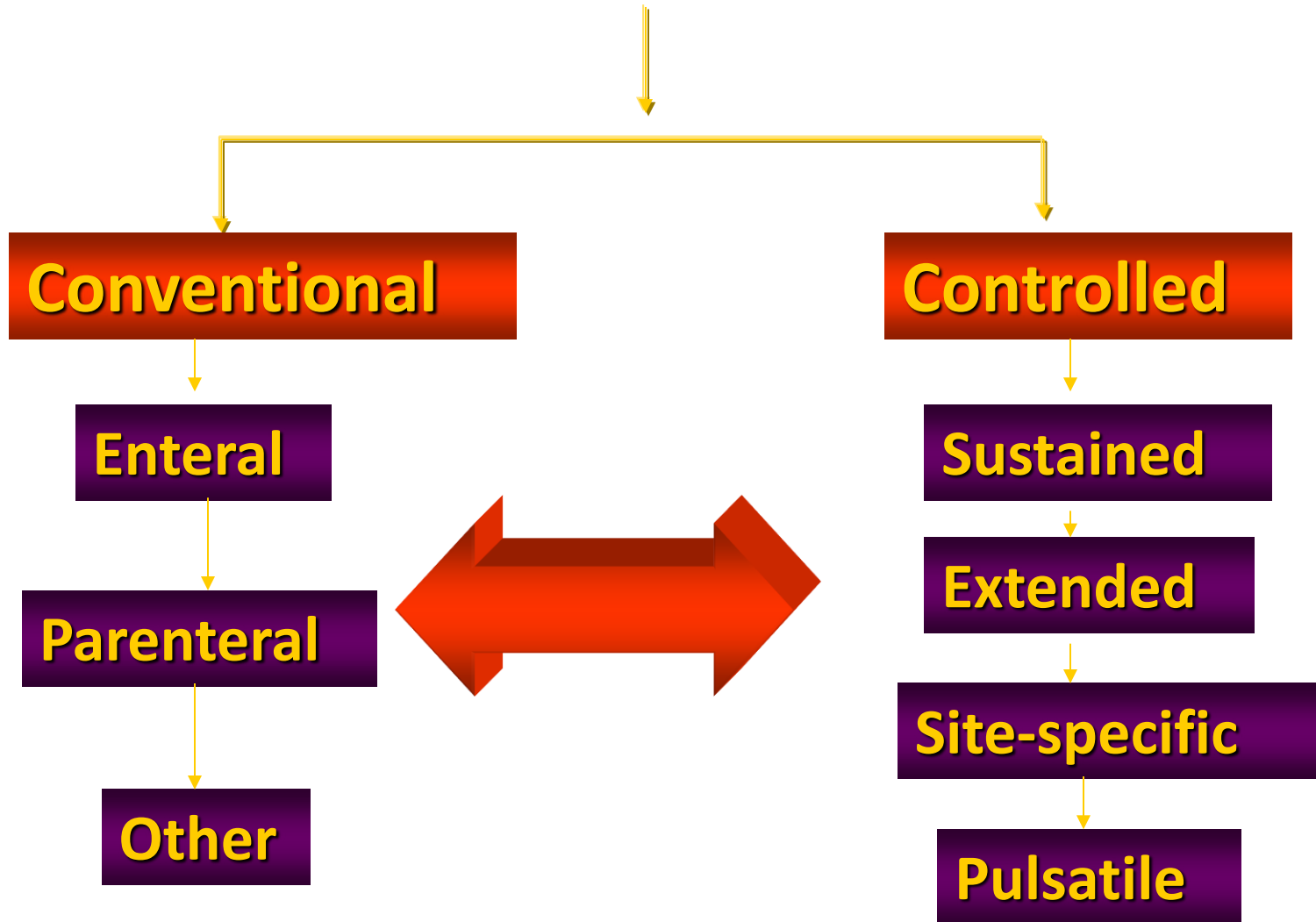
- **Definition**

- The appropriate administration of drugs through various routes in the body for the purpose of improving health
- It is highly interdisciplinary
- It is not a young field
- It has recently evolved to take into consideration
 - Drug physico-chemical properties
 - Body effects and interactions
 - Improvement of drug effect
 - Patient comfort and well being

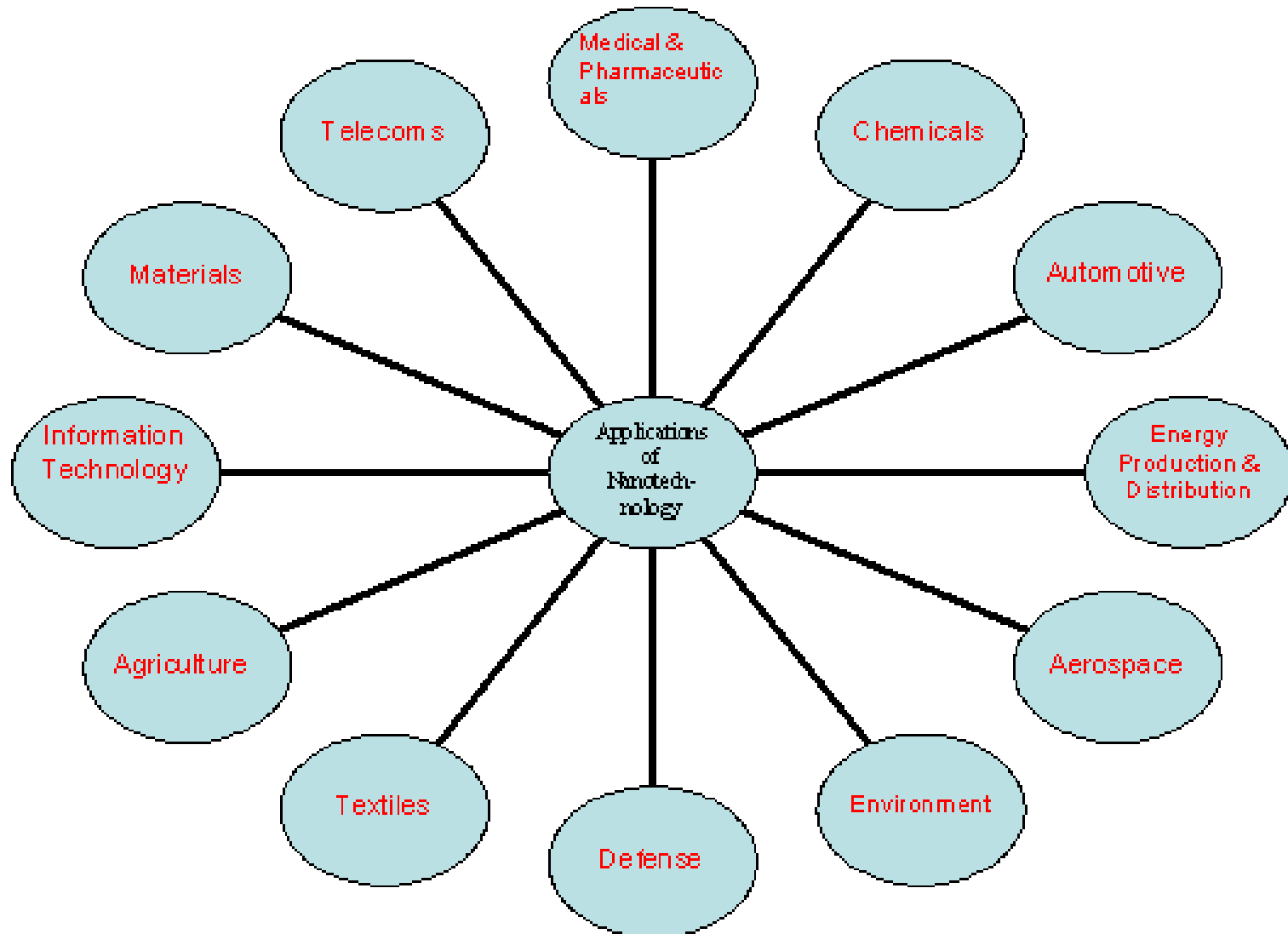


**Controlled
Drug Delivery**

Drug Delivery



Applications of Nanotechnology



Nanoparticles for Drug Delivery

- Metal-based nanoparticles
- Lipid-based nanoparticles
- Polymer-based nanoparticles
- Biological nanoparticles

Nanobiopharmaceuticals

- In biopharmaceuticals, in addition to the main technologies covered-liposomal, monoclonal antibody-based, and polymer-based technologies host of newer technologies such as nanoparticles including various nanodimensional entities such as molecular imprinted polymers, metallofullerenes, prodrug delivery, oral, injectable and implantable, pulmonary, and transdermal and transmucosal delivery have come up.

SOME SIGNIFICANT ACHIEVEMENTS OF NANODEVICES

- **Development of one dose a day ciprofloxacin using nanotechnology**
- **Tumor targeted taxol delivery using nanoparticles in Phase 2 clinical trial stage**
- **Improved ophthalmic delivery formulation using smart hydrogel nanoparticles**
- **Oral insulin formulation using nanoparticles carriers.**
- **Liposomal based Amphotericin B formulation**

PRIORITY AREAS

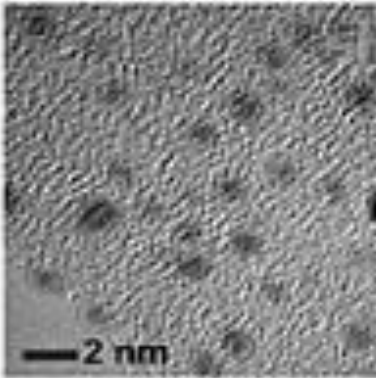
- **Cancer Nanotechnology**
 - (i) Diagnosis using Quantum Dots**
 - (ii) Tumor Targeted Delivery**
 - (iii) Imaging**
 - (iv) Cancer Gene Therapy**

Nanopowder

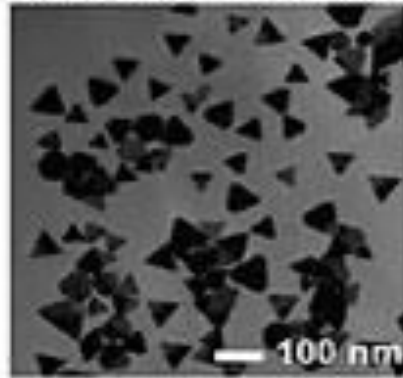
- Nanopowders are powders composed of nanoparticles, that is particles having an average diameter below 50 nanometers (nm).
- A jar of a true nanopowder when emptied from chest height to toward the floor will disperse into the air before reaching the floor.
- Most manufacturers of “nanopowders” produce micropowder assemblies of nanoparticles but the powder itself is rarely a nanopowder.
- Such compounds have two or more different cations (positively charged elements) in their chemical formula. An example of a complex compound is calcium titanate (CaTiO_3).

Nanocluster

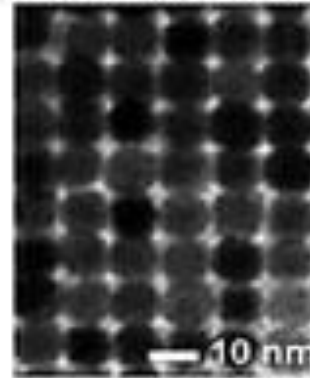
Au nanoclusters
(~1 nm diameter)



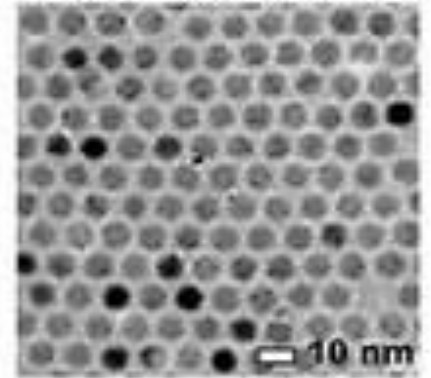
Ag nanoprisms
(edge length ~90 nm)



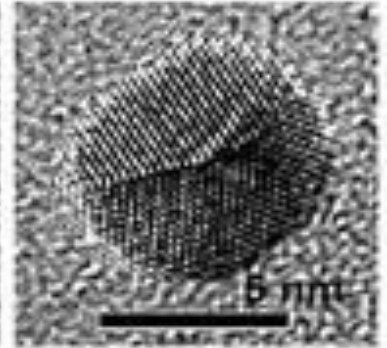
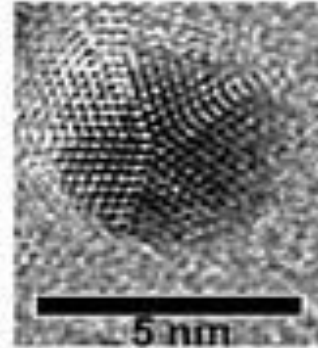
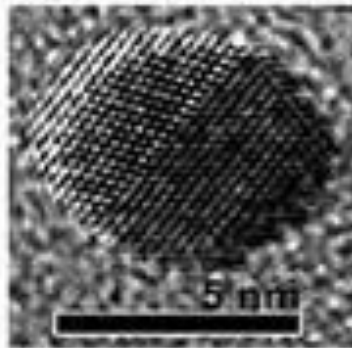
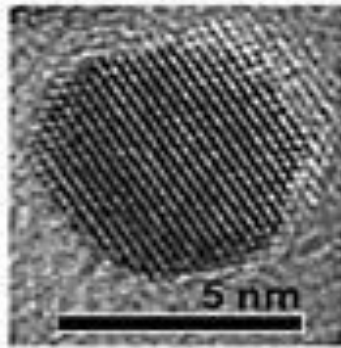
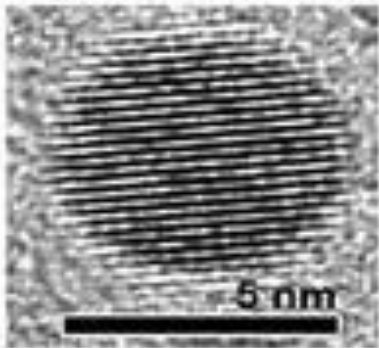
Square superlattice
of 10 nm Ag particles



Hexagonal superlattice
of 6 nm Au particles



High resolution TEM images of Au and Ag nanoparticles:



Nanocluster

- One of the central themes in nanoscience research is to synthesize high quality nanoparticles with precise control over particle size, shape, structure, and composition.
- For inorganic nanoparticles (e.g. metal and semiconductor), two regimes are of particular interest, that is, nanoclusters in a size range from subnanometer to ~ 2 nm and nanocrystals (typically 2-100 nm).

Nanocrystals

NanoCrystal® particles have increased surface area

Total surface area 6cm^2



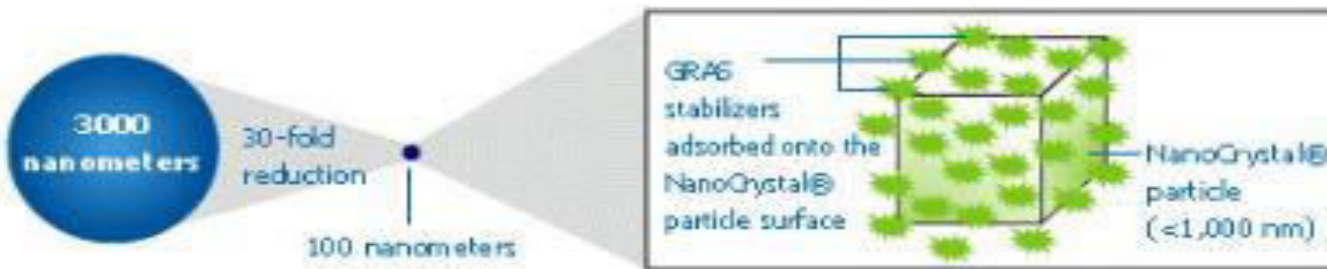
Total surface area 12cm^2



Total surface area 24cm^2



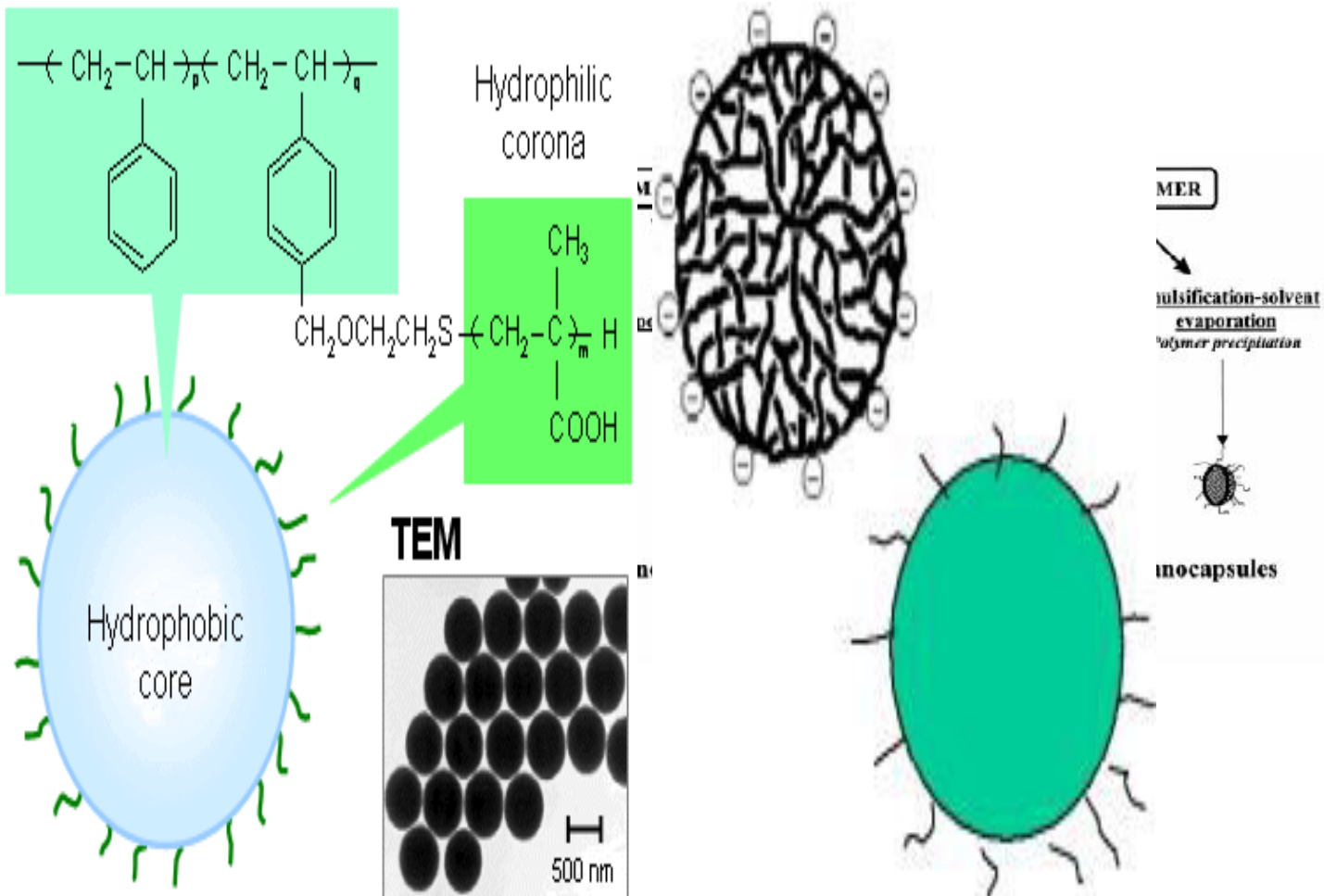
Micronization vs. Nanonization™ process



Nanocrystals

- **When the size of the material is reduced to less than 100 nanometers, the realm of quantum physics takes over and materials begin to demonstrate entirely new properties.**
- **Nano-design of drugs by various techniques like milling, high pressure homogenization, controlled precipitation etc., are explored to produce, drug nanocrystals, nanoparticles, nanoprecipitates, nanosuspensions (which for ease of understanding commonly mentioned as nanocrystals).**
- **As decreased size will increase the solubility of drugs hence, this technology is explored to increase oral bioavailability of sparingly water soluble drugs.**

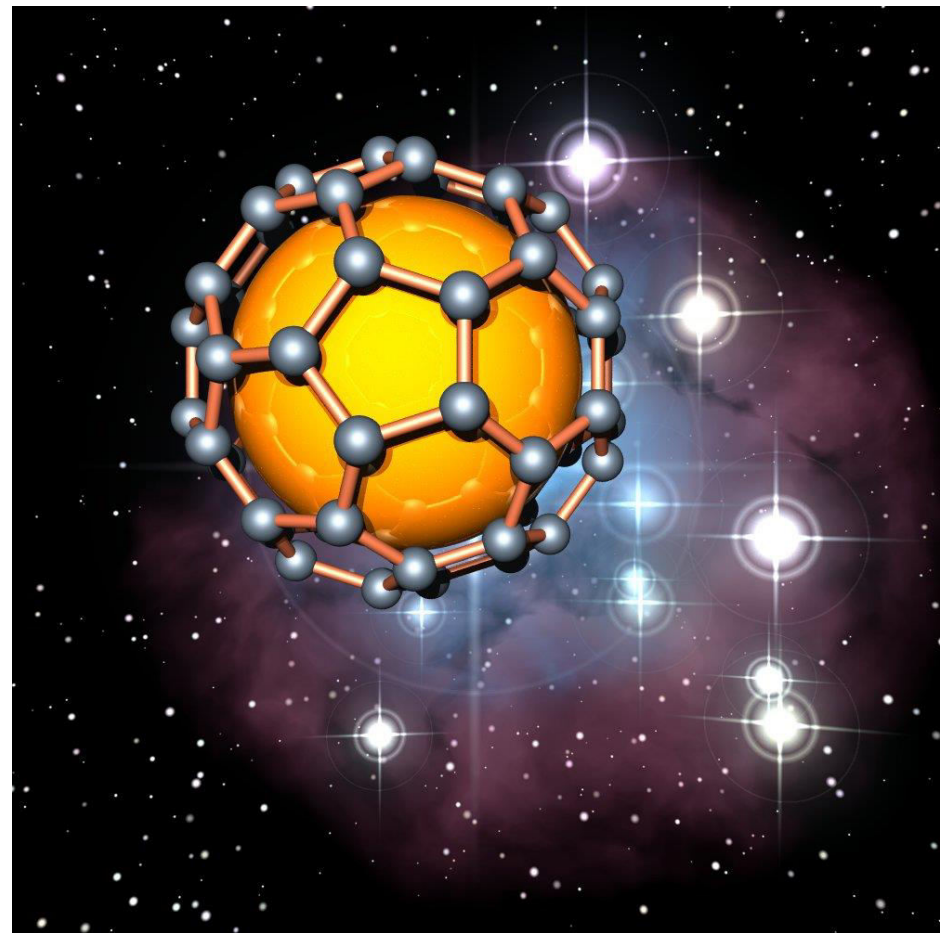
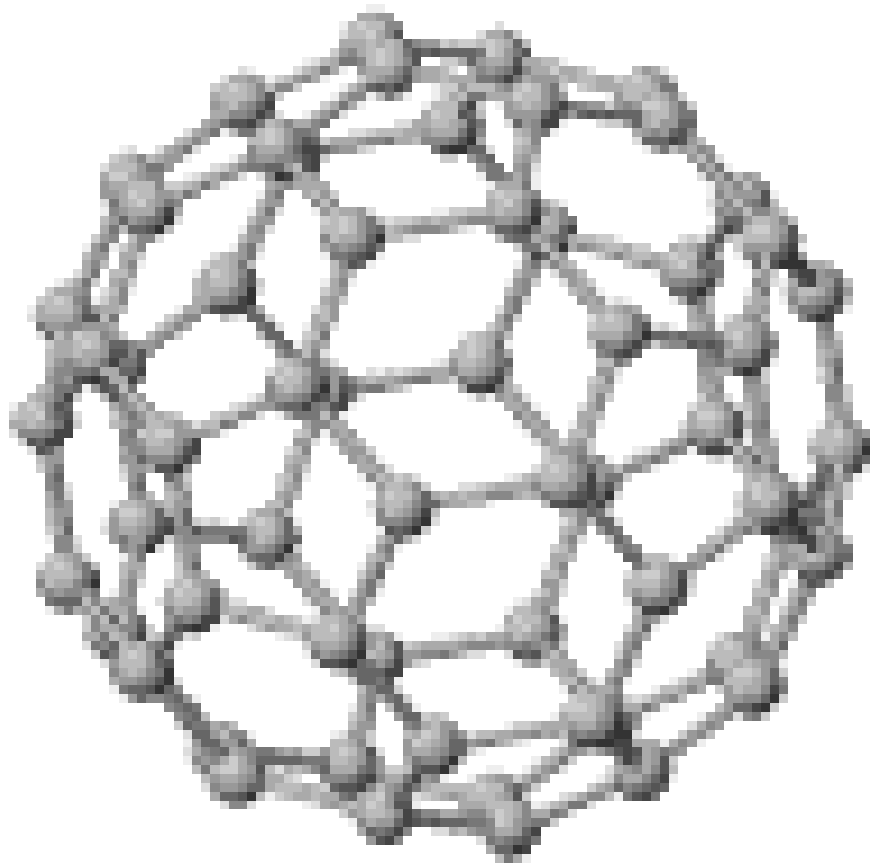
Polymeric Nanoparticles



Polymeric Nanoparticles

- In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices in view of their applications in drug targeting to particular organs/tissues, as carriers of DNA in gene therapy, and in their ability to deliver proteins, peptides and genes through a per oral route of administration.

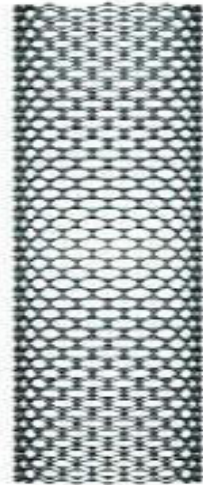
Carbon 60



Carbon 60

- C60 are spherical molecules about 1nm in diameter, comprising 60 carbon atoms arranged as 20 hexagons and 12 pentagons: the configuration of a football.
- Hence they find application as NanoPharmaceuticals with large drug payload in their cage like structure.
- On the other hand with development of various chemical substitutes for C60, it is possible to develop functionalized C60 with better drug targeting properties

Carbon Nanotube



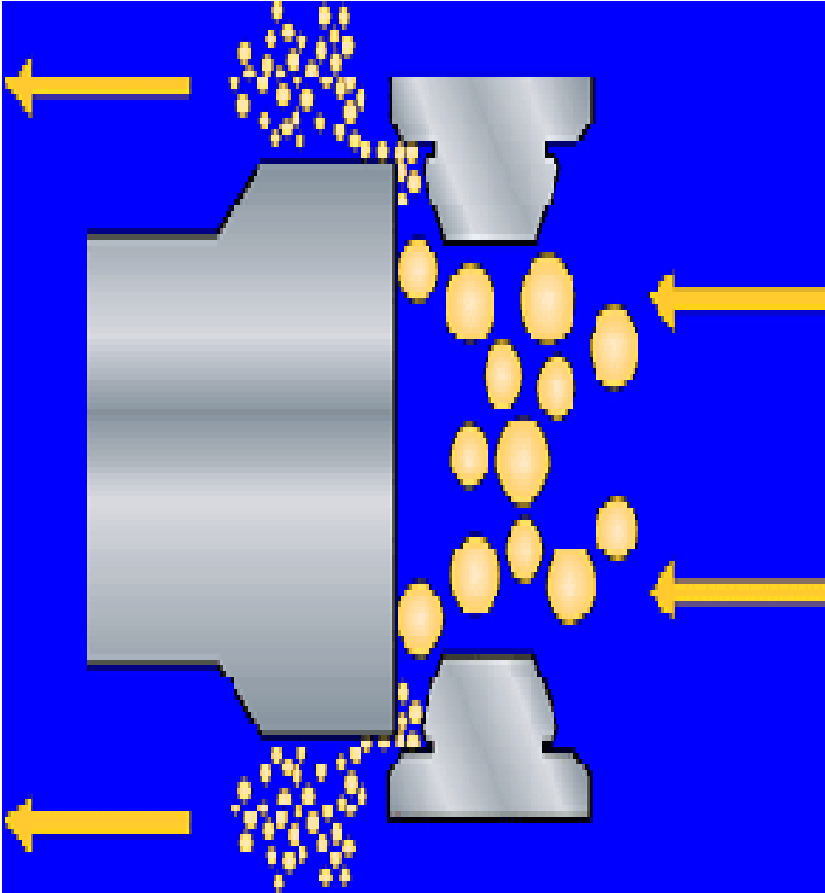
Carbon Nanotube

- Carbon nanotubes are adept at entering the nuclei of cells and may one day be used to deliver drugs and vaccines.
- The modified nanotubes have so far only been used to ferry a small peptide into the nuclei of fibroblast cells.
- But the researchers are hopeful that the technique may one day form the basis for new anti-cancer treatments, gene therapies and vaccines.

Equipment's for Nanoparticles

1. Homogenizer
2. Ultra Sonicator
3. Mills
4. Spray Milling
5. Supercritical Fluid Technology
6. Electrospray
7. Ultracentrifugation
8. Nanofiltration

Homogenizer & Ultra Sonicator



Oral Administration

- Advantages

- Patient: Convenience, not invasive, higher compliance
- Manufacture: well established processes, available infrastructure

- Disadvantages

- Unconscious patients cannot take dose
- Low solubility
- Low permeability
- Degradation by GI enzymes or flora
- First pass metabolism
- Food interactions
- Irregular absorption

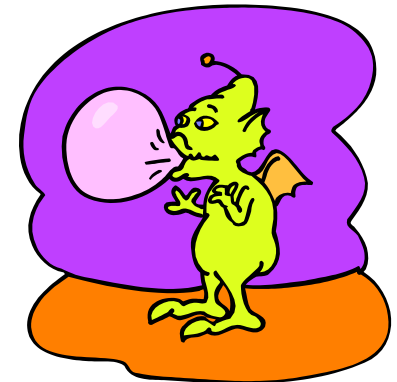
Oral Administration

- Traditional oral delivery systems
 - Tablets
 - Capsules
 - Soft gelatin capsules
 - Suspensions
 - Elixirs



Buccal/Sublingual

- Advantages
 - By-pass First pass metabolism
 - Rapid absorption
 - Low enzymatic activity
- Disadvantages
 - Discomfort during dissolution
 - Probability of swallowing- lost of effect
 - Small doses
- Traditional delivery system/devices
 - Tablets
 - Chewing gum

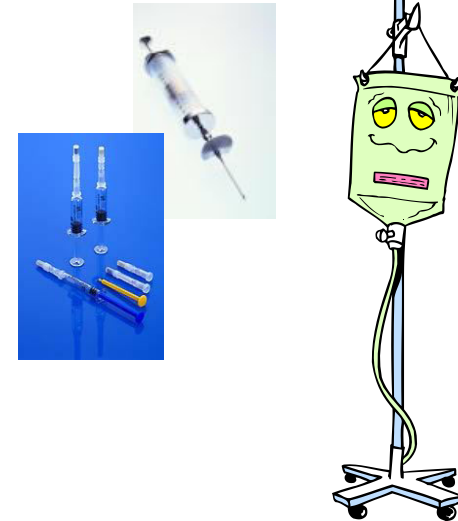


Rectal

- Advantages
 - By-pass first pass metabolism
 - Useful for children
- Disadvantages
 - Absorption depends on disease state
 - Degradation by bacterial flora
 - Uncomfortable
- Traditional delivery system/devices
 - Suppository
 - Enema

Intravenous (IV)

- **Advantages**
 - Drug 100% bioavailable
 - Rapid response
 - Total control of blood concentration
 - Maximize incorporation of degradable drugs
 - By-pass FPM
- **Disadvantages**
 - Invasive
 - Trained personnel
 - Possible toxicity due to incorrect dosing
 - sterility
- **Traditional delivery system/devices**
 - Injection-bolus
 - IV bag - infusion



Subcutaneous

- Advantages
 - Patient self-administration
 - Slow, complete absorption
 - By-pass FPM
- Disadvantages
 - Invasive
 - Irritation, inflammation
 - Maximum dose volume - 2mL

Intramuscular

- Advantages
 - Patient can administer the drug himself
 - Larger volume than subcutaneous
 - By-pass first pass metabolism
- Disadvantages
 - Invasive – patient discomfort
 - Irritation, inflammation
 - May require some training

Inhalers

- Advantages
 - By-pass FPM
 - Gases are rapidly absorbed
- Disadvantages
 - Solids and liquids can be absorbed if size is below 0.5um

Transdermal

- Advantages
 - Local effect
 - Ease of administration
- Disadvantages
 - Low absorption for some drugs
 - May cause allergic reactions
- Requirements
 - Low dosage <10 mg/mL
 - MW < 1,000



Factors Influencing the Selection of the Delivery Route

- **Drug physico-chemical properties**
 - **Drug molecular size (molecular weight)**
 - **Half-life**
 - **Chemical stability**
 - **Loss of biological activity in aqueous solution**
 - **Proteins**
 - **Denaturation, degradation**

Factors Influencing the Selection of the Delivery Route

- Solubility in aqueous solution (hydrophobicity/hydrophilicity)**
 - pH**
 - pKa - ionization**
 - Temperature**
 - Concentration**
 - Crystallinity**
 - Particle size**
 - State of hydration**

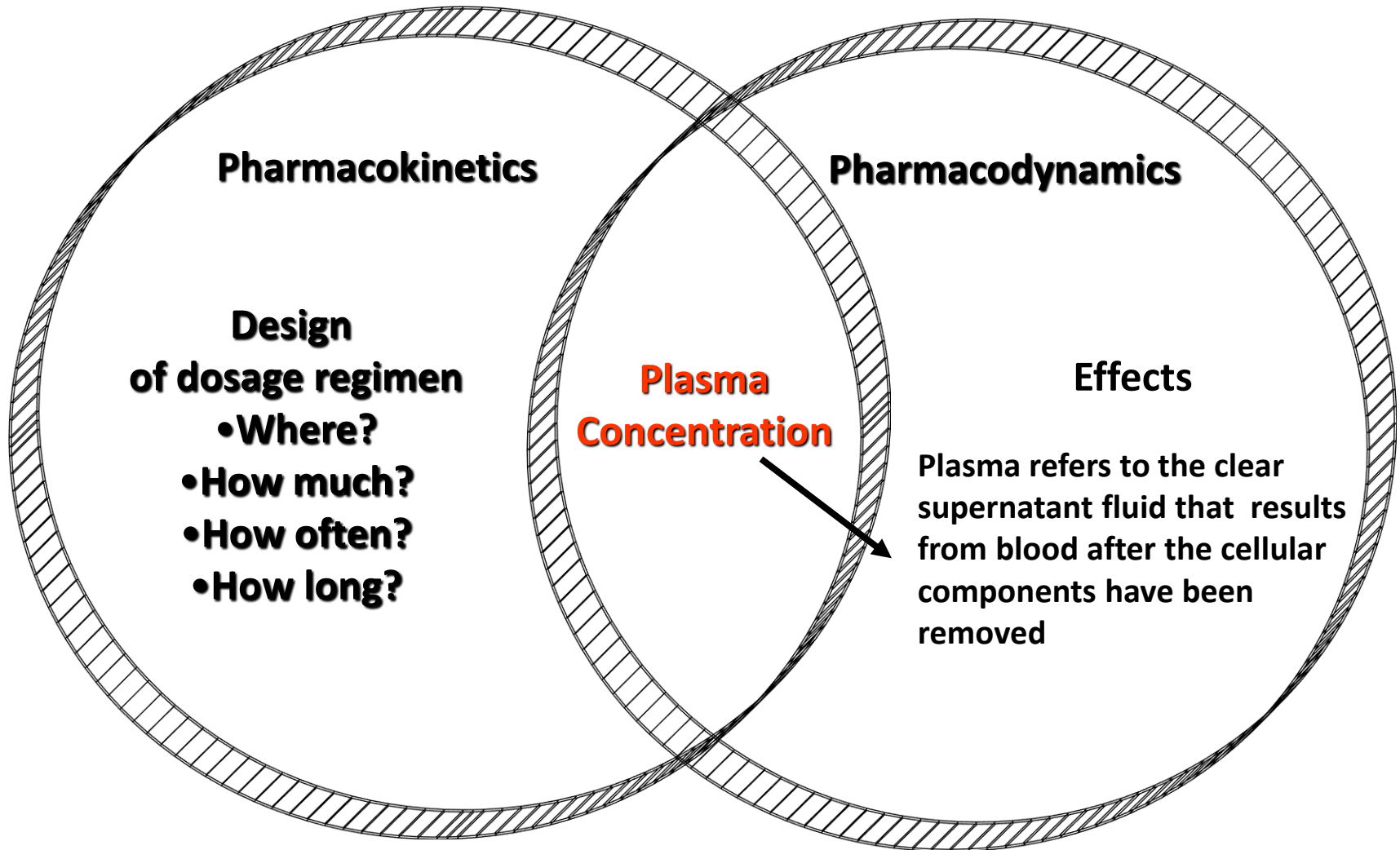
Factors Influencing the Selection of the Delivery Route

- Drug biological interactions
 - Sensitive to FPM
 - Low membrane permeability
 - Efflux pumps (MRP, MDR) – cancer drugs
 - Hydrophilicity
 - High-density charge
 - Enzymatic degradation
 - Bacterial degradation
 - Half-life
 - Side effects
 - Irritation

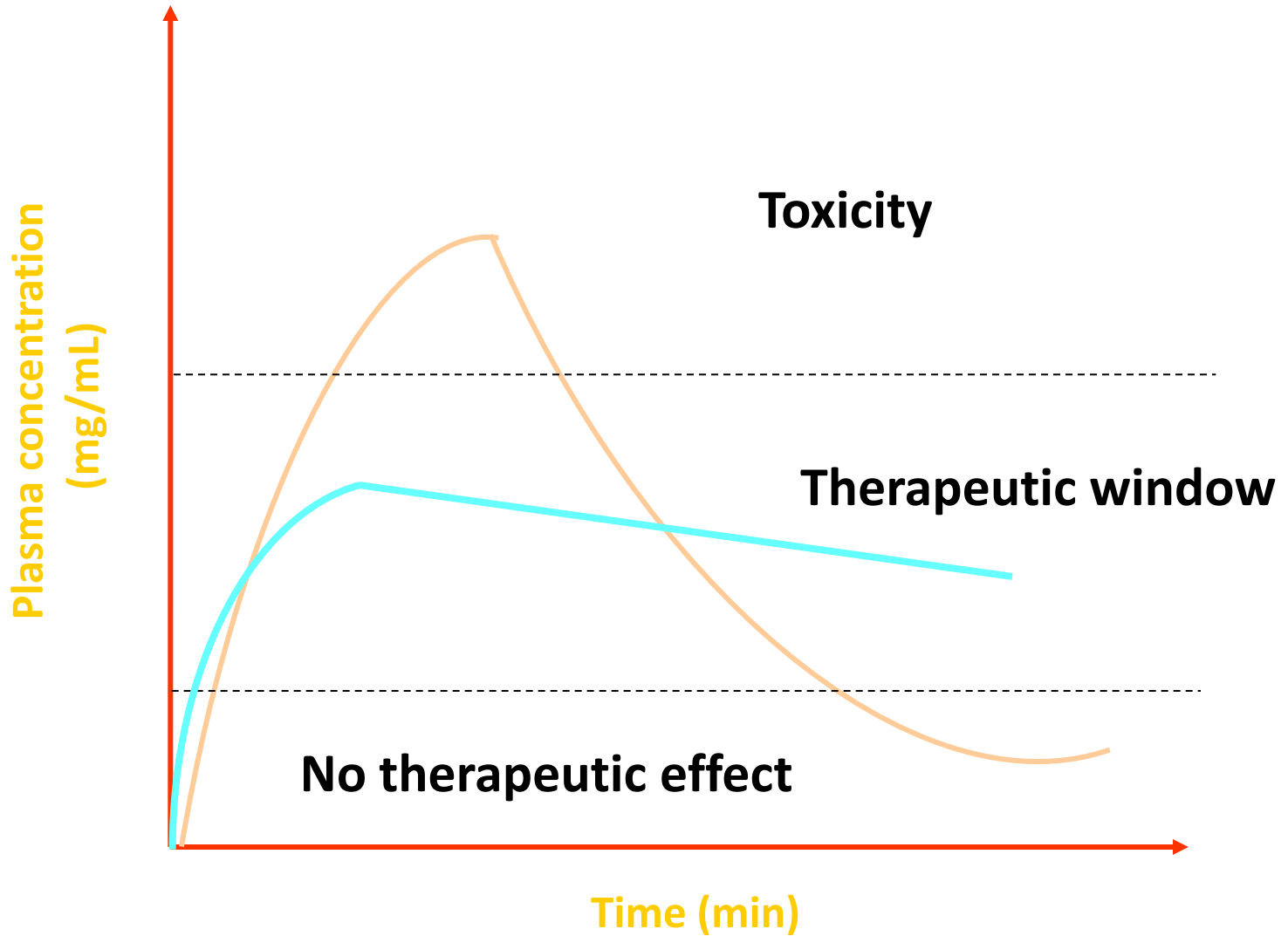
Factors Influencing the Selection of the Delivery Route

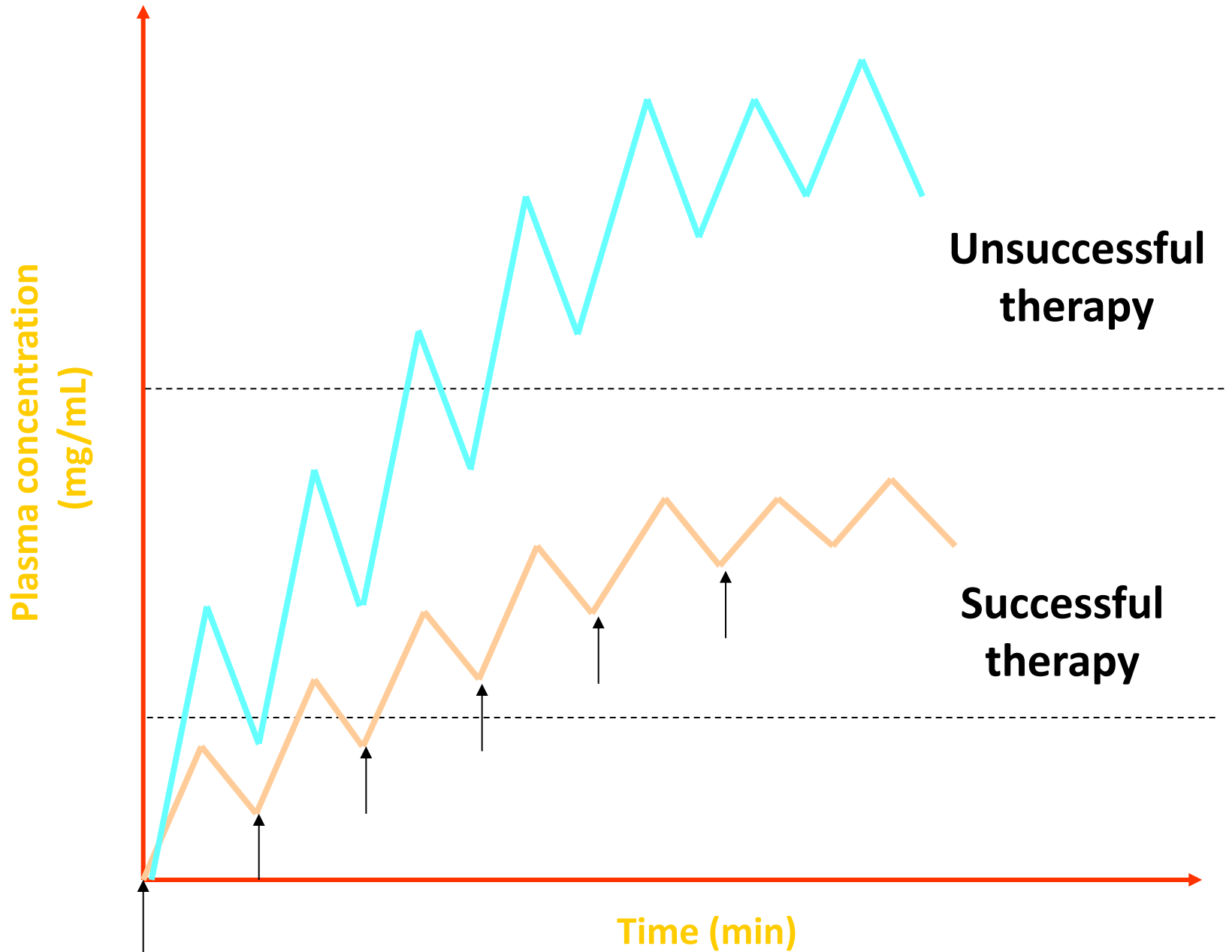
- **Desired pharmacological effect**
 - **Local**
 - topical, vaginal
 - **Systemic**
 - oral, buccal, IV, SC, IM, rectal, nasal
 - **Immediate response**
 - IV, SC, IM, nasal
 - **Dose size**
 - **Drug molecular size**

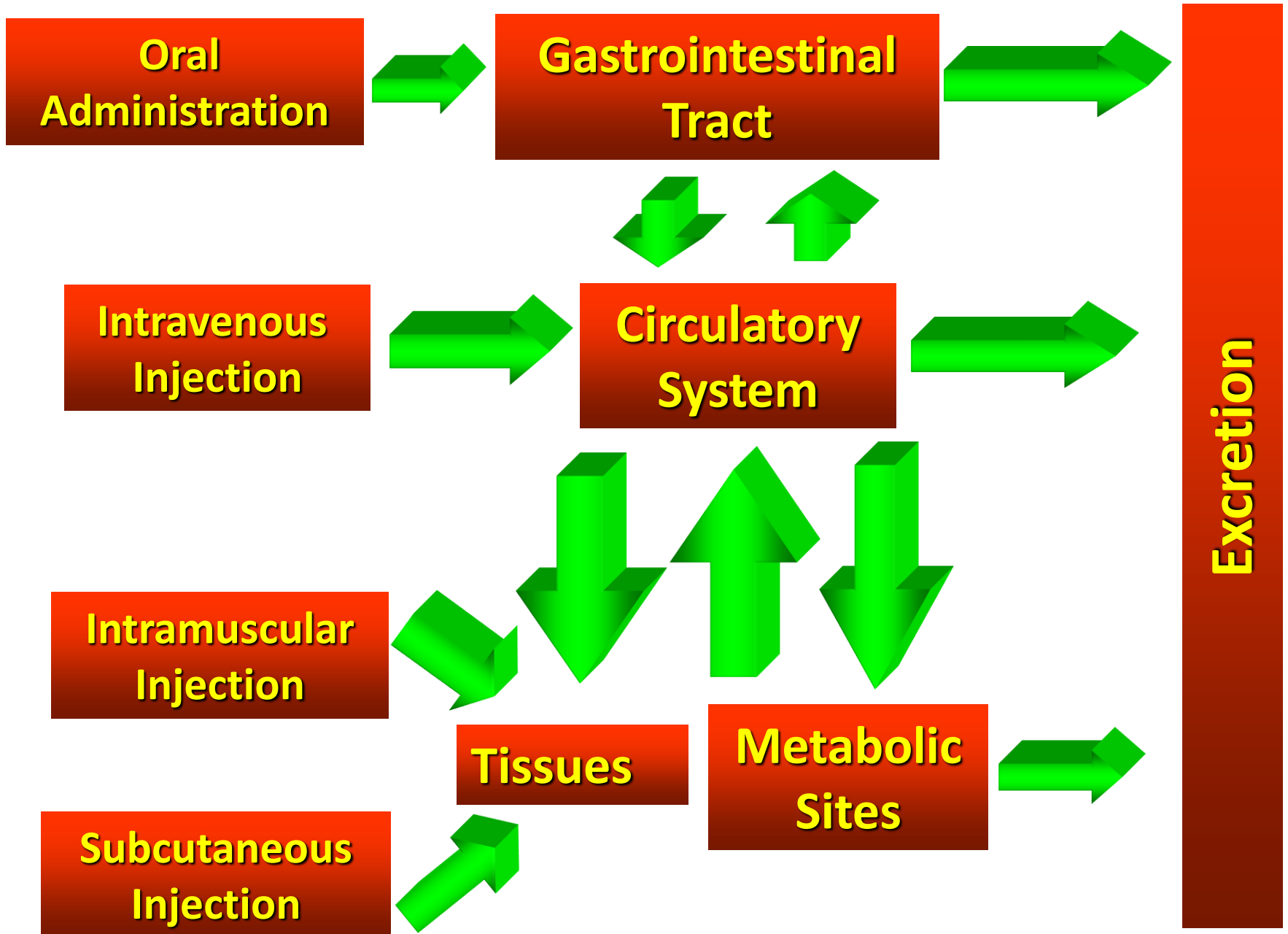
Pharmacokinetics and Pharmacodynamics



Plasma Concentration





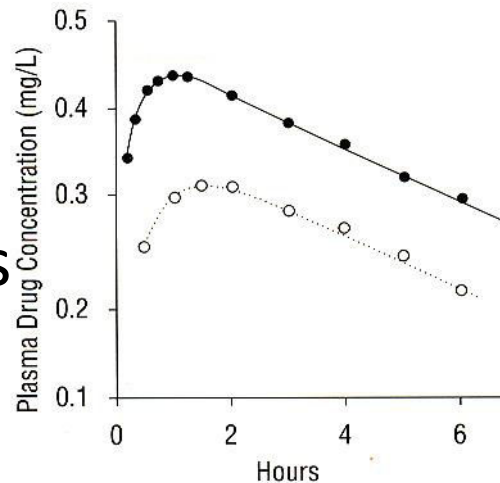


Absorption of drugs could vary within different administration routes

- 500 mg dose given
 - intramuscularly
 - orally

**to the same subject on separate occasions

- Biological barriers greatly affect the extent of drug absorption



Journal of Nanomedicine & Biotherapeutic Discovery

- Journal of Nanomedicine & Biotherapeutic Discovery
- Journal of Nanomedicine & Nanotechnology

Journal of Nanomedicine & Biotherapeutic Discovery

- International Conference on Nanotek & Expo
- International Conference on Signal Processing



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