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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)


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


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

Conventional
- Enteral
- Parenteral
- Other

Controlled
- Sustained
- Extended
- Site-specific
- Pulsatile
Applications of Nanotechnology

- Telecoms
- Medical & Pharmaceuticals
- Chemicals
- Automotive
- Energy Production & Distribution
- Aerospace
- Environment
- Defense
- Textiles
- Agriculture
- Information Technology
- Materials
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 (CaTiO3).
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:
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
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

Hydrophobic core

Hydrophilic corona

TEM

Schematic representation of a polymeric nanoparticle with a hydrophobic core and a hydrophilic corona.
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 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
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
  • Crystalinity
  • 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

Pharmacokinetics
- Design of dosage regimen
  - Where?
  - How much?
  - How often?
  - How long?

Pharmacodynamics
- Effects

Plasma Concentration

Plasma refers to the clear supernatant fluid that results from blood after the cellular components have been removed.
Plasma Concentration

<table>
<thead>
<tr>
<th>Plasma Concentration (mg/mL)</th>
<th>Time (min)</th>
<th>Therapeutic window</th>
<th>Toxicity</th>
<th>No therapeutic effect</th>
</tr>
</thead>
</table>

Graph showing the relationship between plasma concentration and time, indicating the therapeutic window, toxicity, and no therapeutic effect.
Oral Administration

Intravenous Injection

Intramuscular Injection

Subcutaneous Injection

Gastrointestinal Tract

Circulatory System

Tissues

Metabolic Sites

Excretion
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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