CHAPTER NINE

Drug Delivery

Nanotechnology in drug delivery

Nanotechnology received a lot of attention with the never-seen-before enthusiasm because of its future potential that can literally revolutionize each field in which it is being exploited. In drug delivery, nanotechnology is just beginning to make an impact. Many of the current "nano" drug delivery systems, however, are remnants of conventional drug delivery systems that happen to be in the nanometer range, such as liposomes, polymeric micelles, nanoparticles, dendrimers, and nanocrystals. Liposomes and polymer micelles were first prepared in 1960's, and nanoparticles and dendrimers in 1970's. Colloidal gold particles in nanometer sizes were first prepared by Michael Faraday more than 150 years ago, but were never referred to or associated with nanoparticles or nanotechnology until recently. About three decades ago, colloidal gold particles were conjugated with antibody for target specific staining, known as immunogold staining. Such an application may be considered as a precursor of recent explosive applications of gold particles in nanotechnology. The importance of nanotechnology in drug delivery is in the concept and ability to manipulate molecules and supramolecular structures for producing devices with programmed functions. Conventional liposomes, polymeric micelles, and nanoparticles are now called "nanovehicles," and this, strictly speaking, is correct only in the size scale. Those conventional drug delivery systems would have evolved to the present state regardless of the current nanotechnology revolution. To appreciate the true meaning of nanotechnology in drug delivery, it may be beneficial to classify drug delivery systems based on the time period representing before and after the nanotechnology revolution.

To describe what nanotechnology can do to manufacture nano/micro drug delivery systems, one can use manufacturing of nano/micro particles (or capsules) as an example. The current methods of preparing nano/micro particles are mainly based on double emulsion methods or solvent exchange technique. The main problems with the current methods are the low drug loading capacity, low loading efficiency, and poor ability to control the size distribution. Utilizing nanotechnologies, such as nanopatterning, could allow manufacturing of nano/micro particles with high loading efficiency and highly homogeneous particle sizes.

Using nanotechnology, it may be possible to achieve

(1) improved delivery of poorly water-soluble drugs (Uptake of low solubility drugs)

(2) targeted delivery of drugs in a cell- or tissue-specific manner (Delivery of drugs specifically to the target site)

(3) transcytosis of drugs across tight epithelial and endothelial barriers

(4) delivery of large macromolecule drugs to intracellular sites of.

(5) Drug bioavailability

Therapy typically involves delivering drugs to a specific target site. If an internal route for drug delivery is not available, external therapeutic methods, such as radiotherapy and surgical procedures are employed. Nanotechnologies are making a compelling contribution in this area through the development of novel modes for drug delivery, and some of these methods have proven effective in a clinical setting and are clinically used. For example, doxorubicin a drug which exhibits high toxicity, can be delivered directly to tumour cells using liposomes (Doxil®) without affecting the heart or kidneys. Additionally, paclitaxel incorporated with polymeric mPEG-PLA micelles (Genexol-PM®) are used in chemotherapeutic treatment of metastatic breast cancers.

The success of nanotechnologies in drug delivery can be attributed to the improved in:

- vivo distribution
- evasion of the reticuloendothelial system
- the favourable pharmacokinetics

What are the elements of a perfect drug delivery system?

- Control over drug release
- The targeting ability

Side effects can be reduced significantly, and drug efficiency can be ensured by specifically targeting and killing harmful or cancerous cells.

What are the Benefits of nanoparticle drug delivery systems?

- Minimised irritant reactions
- Improved penetration within the body due to their small size
- Allowing for intravenous and other delivery routes

The specificity of nanoparticle drug delivery systems is made possible by attaching nano-scaled radioactive antibodies that are complementary to antigens on the cancer cells with drugs

Table II Comparison of nanoparticles and fine particles in drug delivery systems

Nanoparticles	Fine particles
Increased bioavailability	Low bioavailability
Dose proportionality	Potential toxic effects
Decreased toxicity	Larger and unstable dosage form
Smaller dosage form	Low agent surface area hence low dissolution rate
Large agent surface area hence high dissolution rate	

Nanotechnology and cancer treatment

Staggering numbers of individuals suffer from cancer worldwide, highlighting the need for an accurate detection method and novel drug delivery system that is more specific, efficient and exhibits minimal side effects.

Anticancer treatments are often regarded as superior if the therapeutic agent can reach the specific target site without resulting in any side effects. Chemical modifications of the surface of nanoparticle carriers may improve this required targeted delivery. One of the best examples of modifications at the surface of nanoparticles is the incorporation of PEG or polyethylene oxide.

What are the advantages of the incorporation of PEG with nanoparticles?

- Enhance the specificity of drug uptake
- The tumour-targeting ability
- Avoids the detection of nanoparticles as foreign objects by the body's immune system
- Allowing nanoparticles to circulate in the bloodstream until they reach the tumour

Additionally, the application of hydrogel in breast cancer is a prime example of this innovative technology. Herceptin is a type of monoclonal antibody used in breast cancer treatment by targeting human epidermal growth factor receptor 2 (HER2) on cancer cells. A vitamin E-based hydrogel has thus been developed that can deliver Herceptin to the target site for several weeks with just a single dose. Due to the improved retention of Herceptin within the tumour, the hydrogel-based drug delivery is more efficient than conventional subcutaneous and intravenous delivery modes, thus making it a better anti-tumour agent.

What are the reasons for modified nanoparticles through the use of nanotechnologies?

- prolong circulation
- enhance drug localization
- increase drug efficacy
- potentially decrease the development of multidrug resistance through the use of nanotechnologies