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Role Of Nanotechnology In New Drug Delivery Systems

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To the Editor

Nanotechnology is the study, design, creation, synthesis, manipulation, and application of materials, devices, and systems at the nanometre scale. The prefix *nano* is derived from the Greek word *dwarf*. One nanometer (nm) is equal to one-billionth of a meter, that is, 10^{-9} m. This size range holds so much interest as in this range materials can have different and enhanced properties compared with the same material at a larger size.

Nanomaterials differ significantly from other materials due to the following two major principal factors: the increased surface area and quantum effects. These factors can enhance properties such as reactivity, strength, electrical characteristics and in vivo behaviour. Nanotechnology and nanoscience are widely seen as having a great potential to bring benefits to many areas of research and applications. The application of nanotechnology in the field of health care has come under great attention in recent times. There are many treatments today that take a lot of time and are also very expensive. Using nanotechnology, quicker and much cheaper treatments can be developed. There is another aspect for using nanotechnology. Normally, drugs work through the entire body before they reach the disease affected area. Using nanotechnology, the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side-effects.

We have recently seen the launch of the first nano-delivery system (DOXIL; Ortho-Biotec), a reformulated version of the anticancer agent doxorubicin. Here the drug is encased within polyethylene glycol (PEG)-coated liposomes less than 200nm in diameter. Because of the sustained release of the drug from the liposome and its long circulation time from the "stealth" ability conferred by the PEG, intravenous treatment is only required every four weeks. The use of PEG to mask a drug from our natural defences has also been used for antibody based therapeutics.

An ideal drug-delivery system possesses two elements: the ability to target and to control the drug release. Targeting will ensure high efficiency of the drug and reduce the side effects, especially when dealing with drugs that are presumed to kill cancer cells but can also kill healthy cells when delivered to them. The reduction or prevention of side effects can also be achieved by controlled release. NPDDS provide a better penetration of the particles inside the body as their size allows delivery via intravenous injection or other routes. The nanoscale size of these particulate systems also minimizes the irritant reactions at the injection site. Early attempts to direct treatment to a specific set of cells involved attaching radioactive substances to antibodies specific to markers displayed on the surface of cancer cells. Antibodies are the body's means of detecting and flagging the presence of foreign substances. Antibodies specific to certain proteins can be mass produced in laboratories, ironically using the cancer cells. These approaches have yielded some good results, and NPDDSs are demonstrating lot of potential in this area.

Nanoparticles can be used in targeted drug delivery at the site of disease to improve:

- the uptake of poorly soluble drugs
- the targeting of drugs to a specific site
- drug bioavailability

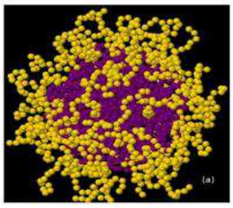
Advantages of Nanoparticles

- Increased bioavailability
- Dose proportionality
- Decreased toxicity
- Smaller dosage form (i.e., smaller tablet)
- Stable dosage forms of drugs which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosage forms.
- Increased active agent surface area results in a faster dissolution of the active agent in an aqueous environment, such as the human body. Faster dissolution generally equates with greater bioavailability, smaller drug doses, less toxicity.
- Reduction in fed/fasted variability.

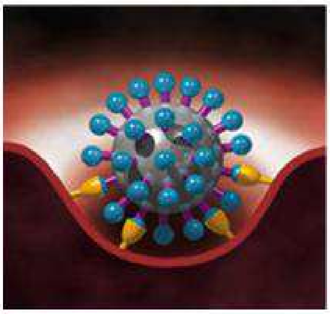
Several anti-cancer drugs including paclitaxel, doxorubicin, 5-fluorouracil and dexamethasone have been successfully formulated using nanomaterials. Polylactic/glycolic acid (PLGA) and polylactic acid (PLA) based nanoparticles have been formulated to encapsulate dexamethasone, a glucocorticoid with an intracellular site of action. Dexamethasone is a chemotherapeutic agent that has anti-proliferative and anti-inflammatory effects. The drug binds to the cytoplasmic receptors and the subsequent drug-receptor complex is transported to the nucleus resulting in the expression of certain genes that control cell proliferation. These drug-loaded nanoparticle formulations that release higher doses of drug for prolonged period of time completely inhibited proliferation of vascular smooth muscle cells.

Colloidal drug delivery modalities such as liposomes, micelles or nanoparticles have been intensively investigated for their use in cancer therapy. The effectiveness of drug delivery systems can be attributed to their small size, reduced drug toxicity, controlled time release of the drug and modification of drug pharmacokinetics and biological distribution. Too often, chemotherapy fails to cure cancer because some tumour cells develop resistance to multiple anticancer drugs. In most cases, resistance develops when cancer cells begin expressing a protein, known as p-glycoprotein that is capable of pumping anticancer drugs out of a cell as quickly as they cross through the cell's outer membrane. New research shows that nanoparticles may be able to get anticancer drugs into cells without triggering the p-glycoprotein pump.

It is to be seen that many of the current "nano" drug delivery systems are remnants of conventional drug delivery systems that happen to be in the nanometer range, such as liposomes, polymeric micelles, nanoparticles, dendrimers and nanocrystals.



Self assembled Pluronic micelle



Dendrimer

Examples of drug delivery technologies in relation to the current nanotechnology revolution.

Nanotechnology is expected to have a revolutionary impact on medicine. Nanoparticles can play a major role in medicine and especially in diagnosis and therapy of cancer, cardiovascular diseases and infectious diseases. To further the application of nanoparticles in pharmacy, it is important that the systems are stable, capable of being functionalized, biocompatible and directed to specific target sites in the body after systemic administration. Nanotechnology is on its way to make a big impact in Pharmaceutical and Medical diagnostics sciences. A dynamic collaboration is observed within the Researchers, Government, Pharmaceutical - Biomedical companies and educational institutions all over the world in developing the nanotechnology applications in advanced medicine and patient care. It is expected that the forthcoming generations of nano products will have target specificity, may carry multiple drugs and could potentially release the payloads at varying time intervals. Pharmaceutical education in India is also taking significant steps in incorporating courses as well as offering specialization in nanotechnology and its applications in Pharmaceutical scenario.

Period	Before Nanotechnology (Past)	Transition Period (Present)	Mature Nanotechnology (Future)
Technology	Emulsion-based preparation of nano/micro particles	Nano/micro fabrication	Nano/micro manufacturing
Examples	• - Liposomes • - Polymer micelles • -Dendrimers • Nanoparticles • Nanocrystals • - Microparticles	• - Microchip systems • - Microneedle transdermal delivery systems • - Layer-by-layer assembled systems • - Microdispensed particles	• - Nano/micro machines for scale-up production

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

Summary of application areas for nanoscale pharmaceuticals and medicine in drug delivery.

Material/technique	Property	Applications
Nanoparticles in the range of 50–100 nm.	Larger particles cannot enter tumour pores while nanoparticles can easily move into a tumour.	Cancer treatment.
Nanosizing in the range of 100–200 nm.	Low solubility.	More effective treatment with existing drugs.
Polymers.	These molecules can be engineered to a high degree of accuracy.	Nanobiological drug carrying devices.
Ligands on a nanoparticle surface.	These molecules can be engineered to a high degree of accuracy.	The ligand target receptors can recognise damaged tissue, attach to it and release a therapeutic drug.
Nanocapsules.	Evading body's immune system whilst directing a therapeutic agent to the desired site.	A Buckyball-based AIDS treatment is just about to enter clinical trials.

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Increased particle adhesion.	Degree of localised drug retention increased.	Slow drug release.
Nanoporous materials.	Evading body's immune system whilst directing a therapeutic agent to the desired site.	When coupled to sensors, drug-delivering implants could be developed.

CONCLUSION:

The emergence of nanotechnology is likely to have a significant impact on drug delivery sector, affecting just about every route of administration from oral to injectable, according to specialist market research firm NanoMarket

Nanotechnology is also opening up new opportunities in **implantable delivery systems**, which are often preferable to the use of injectable drugs, because the latter frequently display first-order kinetics (the blood concentration goes up rapidly, but drops exponentially over time). This rapid rise may cause difficulties with toxicity, and drug efficacy can diminish as the drug concentration falls below the targeted range.

In contrast, implantable time release systems may help minimize peak plasma levels and reduce the risk of adverse reactions, allow for more predictable and extended duration of action, reduce the frequency of re-dosing and improve patient acceptance and compliance.

Nano-implants will also be used in the not-too-distant future for treating cancer. Among the first nanoscale devices to show promise in anti-cancer therapeutics and drug delivery are structures called nanoshells, which NanoMarkets believes may afford a degree of control never before seen in implantable drug delivery products.

Despite these advances, the vast majority of consumers prefer an oral drug delivery system to implantables or injectables. With this in mind, various development groups are working to enhance traditional oral delivery systems with nanoengineered improvements.

There are some areas where nano-enhanced drugs could make a big difference in increasing oral bioavailability and reducing undesirable side effects. By increasing bioavailability, nanoparticles can increase the yield in drug development and more importantly may help treat previously untreatable conditions.

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