

Drug Development and Technology

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As people live longer in the new millennium, it becomes a necessity to develop affordable technologies to improve the quality of life. Because of researchers' ever evolving understanding of human body and with advancement in science and medicine many new life-threatening diseases are coming to light. A successful fight against these diseases and expedition for a long healthy life has led the biotechnology and pharmaceutical industries to develop many new drugs. Delivering these drugs to specific and appropriate tissues of the body is not a trivial issue but can be more important than the drug itself. Rather, it is very crucial to administer the right drug through right route in a right manner into the specific targeted parts of the body.

Drug delivery systems have recently become of great importance to the field of pharmacology as a possible answer to the multitude of problems associated with the safety, efficacy and economic viability of new drugs. Various drug delivery and drug targeting systems are currently under development to offer a host of additional advantages such as ease of administration, increased patient compliance, reduced side effects and minimized drug degradation and loss. By making drugs more palatable, researchers hope to improve patient compliance and even to lower the costs of hospitalization.

Currently, drug delivery techniques focus on moving drugs past our body's barriers and into the blood stream where it will be disseminated to organs and tissues. This is done through various modes of delivery such as oral, injectable, implantable, pulmonary, transdermal etc. Thus, the different routes through which the medicine is administered often influence the drug's success and failure.

Oral route is expected to be the most dominant, followed by the pulmonary route, which is being explored for the delivery of insulin in diabetic patients. Apart from vaccine delivery and anal-

gesics, the nasal route is likely to be particularly useful for the central nervous system applications, since the olfactory region of the nasal cavity could provide a more direct access for targeted drug delivery to the brain. Pulmonary drug release appears to be a feasible option for the delivery of drugs and offers local targeting for the treatment of respiratory diseases. Transdermal drug delivery evades problems such as gastrointestinal irritation, metabolism and interference due to the presence of food. It is appropriate for unconscious patients. As the technique is generally non-invasive it has the advantage of maintaining consistent blood levels.

Conventional forms of drug administration generally rely on pills, eye drops, ointments, and intravenous solutions. Recently, a number of novel drug delivery approaches have been developed which include drug modification by chemical means, drug entrapment in small vesicles that are injected into the bloodstream, and drug entrapment within polymeric materials that are placed in desired bodily compartments. These techniques have already led to delivery systems that improve human health, and continued research may revolutionize the way many drugs are delivered. Most novel drug delivery systems have stemmed work on drug carriers such as polymers, dendrimers, micelles, nanoparticles, etc.

The initial drug delivery systems, earliest introduced in 1970s, were footed on polymers. Now days, polymeric materials still endow with the majority important avenues for investigate, primarily because of their ease of processing and the ability of researchers to readily control their chemical and physical properties via molecular synthesis. Fundamentally, two large categories of polymer systems known as "microspheres" have been considered: reservoir devices and matrix devices. The previous involves encapsulation of a pharma product within a polymer shell, whereas the end describes a system in which a drug is physically entrapped within a polymer network. The drug linked to the polymer slowly diffuses into the bloodstream over a long period. Polymer-linked drugs that are

deliberately oversized can also better target diseased tissues by escaping through leaky microvasculature and then entering cells by endocytosis. A drug-polymer complex can be designed to undergo a conformational change or enzymatic breakdown that results in release of the active drug only under certain conditions.

Bioadhesive polymers help improve the absorption of drugs because they bring the delivery system closer to the mucosa. One can find applications for bioadhesive polymers in almost any region where epithelial cells are found.

As proscribed drug release and subsequent biodegradation are important for developing successful formulations, contemporary research is aimed at investigating biodegradable polymer arrangements. These drug deliverers disintegrate into biologically acceptable compounds, often through the method of hydrolysis, which consequently leaves their incorporated medications behind.

In addition to research on single polymeric networks, researchers are investigating the properties of block copolymers. These supramolecular networks are called polymer micelles which are only tens of nanometers in diameter and therefore ideally sized for enclosing individual drug molecules. Finally, drug release is achieved via common polymer degradation mechanisms, with the specificity of the delivery controlled by the synthetic design.

Furthermore, potential applications of polymer matrixes as drug transport devices have also been studied. It utilizes performing, electro-active polymers as a medium-sensing, bioactive molecule-releasing system. Drug delivery with said conducting polymer membranes is attained through the controlled ionic transport of counter-ions in and out of the membranes.

Conjugation of appropriate biocompatible polymers to bioactive peptides or proteins can decrease toxicity, prevent immunogenic or antigenic side reactions, improve solubility and allow active targeting. The capability of cationic peptide sequences to complex and condense DNA and oligonucleotides proposed prospects for development of non-viral vectors for gene-delivery based on synthetic polymeric hybrid materials.

Relative new materials used for drug delivery are dendrimers, a type of highly branched macromolecule. They are of exacting attention for cancer relevance because of their defined and reproducible size and it is also easy to attach a variety of other molecules to their surface. In addition, while they can be used to encapsulate individual small drug molecules in the manner of polymer micelles, they can also serve as "hubs" onto which large numbers of drug molecules can be attached via covalent bonds.

Recognition capabilities can be built into polymers capable of recognizing certain compounds by using the technique of molecular imprinting. The molecule that the polymer will sense is used as a template around which the monomers are allowed to polymerize and the template molecule is then extracted from the polymer.

Microemulsions are modern colloidal drug carrier systems, which offer several advantages such as ease of preparation, long-term stability, high solubilization capacity for hydrophilic and lipophilic drugs, and improved drug delivery.

The microfabrication field has allowed the creation of microneedles, which have the potential to enable novel devices for gene and drug delivery. Microfabricated neural probes have delivered drugs into neural tissue while simultaneously stimulating and recording neuronal activity, and microneedles have been inserted into arterial vessel walls to deliver antirestenosis drugs. Finally, microhypodermic needles and microneedles for transdermal drug delivery have been developed to reduce needle insertion pain and tissue trauma and to provide controlled delivery across the skin.

The heritable disease that has received the most attention from drug-delivery researchers is diabetes. Over the years, researchers have tried various approaches to introduce insulin into the bloodstream of diabetic patients. Implantable insulin pumps that provide a basal rate of insulin secretion and can be directed by remote control to give doses of insulin at mealtimes may finally become popular.

Furthermore, drug delivery remains an argument in management of cancer and the latest approaches to cancer treatment not only supplement the conventional chemotherapy and radiotherapy but also prevent damage to normal tissues and prevent drug resistance. Pioneering cancer therapies are based on existing models of molecular biology of cancer. These include antiangiogenic agents, immunotherapy, viral oncolysis, targeting of cyclic-dependent kinases and tyrosine kinase receptors, gene therapy etc. Several innovative methods of drug delivery, which include use of microparticles as carriers may be injected into the arterial circulation and guided to the tumor by magnetic field for, targeted drug delivery. Researchers have demonstrated a new way to target and potentially treat tumors where a short piece of protein called pH (Low) Insertion peptide (pHLIP) acts like a nanosyringe to deliver "tags" or therapy to cells. It has been demonstrated that by attaching fluorescent probes and active agents to a pHLIP peptide, tumors could be detected and might be treated as well.

Nanoparticles and nanoformulations have already been applied as drug delivery systems with immense sensation; and they have

still greater potential for many applications, including anti-tumour therapy, gene therapy and radiotherapy, in the delivery of proteins, antibiotics, and vaccines and as vesicles to pass the blood-brain barrier. Nanoparticles afford huge advantages regarding drug targeting, delivery and release and, with their additional potential to combine diagnosis and therapy, emerge as one of the major tools in nanomedicine. Still, the cytotoxicity of nanoparticles or their degradation products ruins a key problem, and improvements in biocompatibility obviously are a main concern of future research.

Thus, modern drug delivery techniques can make possible use of certain chemical entities or biologics that were previously impractical because of toxicities or because they were impossible to administer and hence such innovative systems must be implemented to utilize the specificity and potency of new drugs.

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