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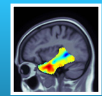
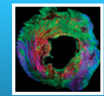
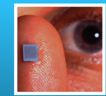
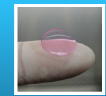
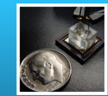






Drug Delivery Systems

Getting Drugs to Their Targets in a Controlled Manner

National Institutes of Health

What are drug delivery systems?

Drug delivery systems are engineered technologies for the targeted delivery and/or controlled release of therapeutic agents.

Drugs have long been used to improve health and extend lives. The practice of drug delivery has changed dramatically in the last few decades and even greater changes are anticipated in the near future. Biomedical engineers have not only contributed substantially to our understanding of the physiological barriers to efficient drug delivery, such as transport in the circulatory system and drug movement through cells and tissues, they have contributed to the development of a number of new modes of drug delivery that have entered clinical practice.

Yet, with all of this progress, many drugs, even those discovered using the most advanced molecular biology strategies, have unacceptable side effects due to the drug interacting with parts of the body that are not the target of the drug. Side effects limit our ability to design optimal medications for many diseases such as cancer, neurodegenerative diseases, and infectious diseases.

Drug delivery systems control the rate at which a drug is released and the location in the body where it is released. Some systems can control both.

How are drug delivery systems used in current medical practice?

Clinicians historically have attempted to direct their interventions to areas of disease or areas at risk for disease. Depending on the medication, the way it is delivered, and how our bodies respond, side effects sometimes occur. These side effects can vary greatly from person to person in type and severity. For example, an oral drug for seasonal allergies may cause unwanted drowsiness or an upset stomach.

Administering drugs locally rather than systemically (affecting the whole body) is a common way to decrease side effects and drug toxicity while maximizing a treatment's impact. A topical (used on the skin) antibacterial ointment for a localized infection or a cortisone injection of a painful joint can avoid some of the systemic side effects of these medications. There are other ways to achieve targeted drug delivery, but some medications can only be given systemically.

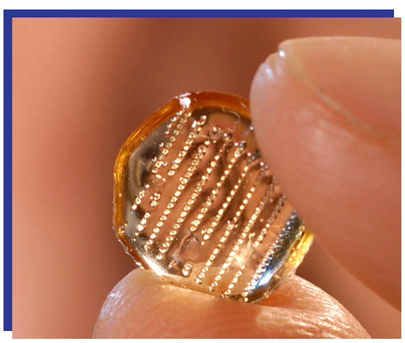


Image of microneedle patch the size of a fingertip used to deliver influenza vaccines.
Source: Dr. Mark Prausnitz, Georgia Institute of Technology

What technologies are NIBIB-funded researchers developing for drug delivery?

Current research on drug delivery systems can be described in four broad categories: routes of delivery, delivery vehicles, cargo, and targeting strategies.

Routes of Delivery

Medications can be taken in a variety of ways—by mouth, by inhalation, by absorption through the skin, or by intravenous injection. Each method has advantages and disadvantages, and not all methods can be used for every medication. Improving current delivery methods or designing new ones can enhance the use of existing medications.

Microneedle arrays are one example of a new method to deliver medications through the skin. In these arrays, dozens of microscopic needles, each far thinner than a strand of hair, can be coated or filled with a medicine. The needles are so small that, although they penetrate the skin, they don't reach nerves in the skin, thus delivering medications painlessly.

NIBIB-funded scientists are developing a microneedle patch for vaccine delivery. These patches are easy to use, do not need to be refrigerated, and don't require special disposal methods, so they could be used by patients themselves at home. Such technology could be especially helpful in rural communities that may not have many health care providers or adequate storage facilities for traditional, refrigerated medicines.

Delivery Vehicles

Just as it's easier to carry a drink in a glass rather than on a plate, finding the right carrier for medications helps to ensure they arrive at their destination intact.

"Nanosponges," created by NIBIB-funded researchers, are a promising vehicle in treating cancer. Comprising a scaffold of tiny, specialized polyester particlescoated with disease-targeting compounds and filled with an anticancer drug, the nanosponges home in on tumors after being injected into the body. Once at their intended site, they safely and slowly degrade, releasing medication at the tumor site at a steady, controlled rate. Early studies have also shown the nanosponges can be used to treat glaucoma, the fourth leading cause of blindness.

By limiting the release of medications throughout the body, the nanosponge and related biotechnologies may revive the use of drugs that were previously unsafe for disease treatment. Beyond broadening treatment options, targeted vehicles for drug delivery may also help to address multi-drug resistant diseases.

Cargo

Perhaps the most obvious route to improving disease treatment would be to focus on the medications themselves. But there are more treatment options than drugs alone. Drug delivery researchers are also exploring the use of genes, proteins, and stem cells as treatments.

One example of a protein treatment is being examined in an NIBIB-funded project to treat autoimmune disorders, in which the body's own defense system mistakenly attacks and destroys healthy tissue. Current treatments generally involve drugs that reduce the overall activity of the immune system, which also increases a person's risk of infections and other illnesses.

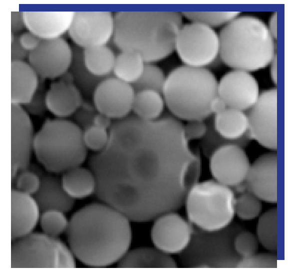
Taking cues from the body's natural process for preventing the immune reaction, the researchers developed microscopic, biodegradable particles that can selectively shut down immune cells associated with the autoimmune disorder multiple sclerosis (MS). Bound with pieces of the protein myelin, the insulating material covering nerve cells that is destroyed in MS, the microparticles were effective at preventing the start of MS in mice and at stopping disease progression when injected after the first sign of illness. The microparticle therapy may also be useful in treating other immune-related conditions, including allergies, or to suppress organ rejection in transplant patients.

Targeting Strategies

Working backwards on a problem can sometimes reveal a solution. In drug delivery research, this means starting with a delivery method that has a known target, which may be whole organs (heart, lung, brain), tissue types (muscle, nerve), disease-specific structures (tumor cells), or structures inside of cells.

NIBIB-funded researchers developed a plant virus nanoparticle that can target and attach itself to prostate cancer cells. When labeled with fluorescent dyes, the viral nanoparticles can show researchers whether cancer cells have spread into bone at earlier stages of the disease than with traditional bone scans.

Made from modified viruses, viral nanoparticles take advantage of the natural ways that viruses have developed to slip past immune defenses and enter cells. This means they do not need to be modified as much as other types of nanoparticles to behave in desired ways, and their actions within the human body are well understood. Plant-based viral nanoparticles are also biodegradable, harmless to humans, easy to use, and cheap to produce.



Tiny biodegradable particles for antigen coupling
Source: Lonnie Shea and Stephen Miller

Further research aims to develop viral nanoparticles that can deliver chemotherapy drugs directly to tumors. Such an advance would reduce the severe side effects usually associated with cancer treatment.

What are some important areas for future research in drug delivery systems?

As scientists study how diseases develop and progress, they are also learning more about the different ways our bodies respond to illness and the influence of specific environmental or genetic cues. Coupled with advances in technology, this increased understanding suggests new approaches for drug delivery research. Key areas for future research include:

Crossing the Blood-Brain Barrier (BBB) in Brain Diseases and Disorders

When working properly, the various cells that comprise the BBB constantly regulate the transfer of essential substances between the bloodstream and the central nervous system as well as recognize and block entry of substances that may harm the brain. Delivering drugs into the brain is critical to the successful treatment of certain diseases such as brain tumors, Alzheimer's disease, and Parkinson's disease, but better methods are needed to cross or bypass the BBB. One method currently under study uses advanced ultrasound techniques that disrupt the BBB briefly and safely so medications can target brain tumors directly, with no surgery required.

Enhancing Targeted Intracellular Delivery

Just as our immune systems defend our bodies against disease, each of our cells also has internal processes to recognize and get rid of potentially harmful substances and foreign objects, which may include drugs enclosed in targeted delivery vehicles. So as researchers work to develop reliable methods of delivering treatments to targeted cells, further engineering is still needed to ensure the treatments reach the correct structures inside cells. Ideally, future health care will incorporate smart delivery systems that can bypass cellular defenses, transport drugs to targeted intracellular sites, and release the drugs in response to specific molecular signals.

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