

A review on advancement in the targeted drug delivery system

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Abstract— Targeted-drug formulations are capable of enhancing the safety, pharmacokinetic profiles and bioavailability of the administered drugs leading to improved therapeutic efficacy compared to conventional therapy therefore Nanoparticle-based drug delivery and imaging platforms have become increasingly popular over the past several decades. Targeted formulations have the ability to improve efficacy and function by positively modulating tissue localization. In this paper we reviewed the development and recent implantation in the targeted drug delivery system.

I. INTRODUCTION

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 past few decades and even greater changes are anticipated in the near future. Biomedical engineers have 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 also contributed to the development several 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 healthy tissues 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.

II. HOW ARE DRUG DELIVERY SYSTEMS USED IN CURRENT MEDICAL PRACTICE

Clinicians historically have attempted to direct their interventions to areas of the body at risk or affected by a 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.

III. ORAL ROUTE OF DRUG DELIVERY

Noninvasive and patient-controlled administration of therapeutics has proved to be the most favored mode of drug administration in the body, especially for chronic therapy. The oral route of administration continues to be the most common method of drug delivery because of some obvious advantages:

- Noninvasive delivery is known to be the safest route for drug administration
- The gastrointestinal tract provides a large surface area for drug absorption.
- Oral administration can be used for delivery of drugs for both local and systemic effects.
- A variety of liquid, solid, and semisolid drug formulations can be administered via the oral route.
- Multiple administrations of drugs are possible with oral delivery.
- Drugs can be self-administered, eliminating the need for hospital admission and trained personnel.
- Oral delivery ensures patient compliance relative to all other routes.
- The drug manufacture process is economical since it can be easily scaled up for mass production.

Often a quick test to evaluate the oral bioavailability of the new chemical entity is to fill the drug into a hard gelatin capsules along with lactose, as this constitutes the simplest formulation for oral administration. In addition to the ease of administration and high patient compliance, the variety of excipients available and relatively lower cost involved in the development of oral dosage forms, favor this route as compared to more invasive approaches. However, oral formulations are not feasible for a variety of new chemical entities (Figure 1). Many of these agents are highly hydrophobic or suffer from stability and permeability constraints, which limit oral bioavailability. Drugs with a

narrow therapeutic index are difficult to administer via the oral route. Additionally several dosage forms (crystalline vs. amorphous drug, type of formulation, rates of disintegration and dissolution, etc.) and physiological factors (gastrointestinal [GI] motility, stability in GI fluid, P-glycoprotein efflux, enzymatic degradation, etc.), contribute to poor bioavailability of certain therapeutic molecules upon oral administration.

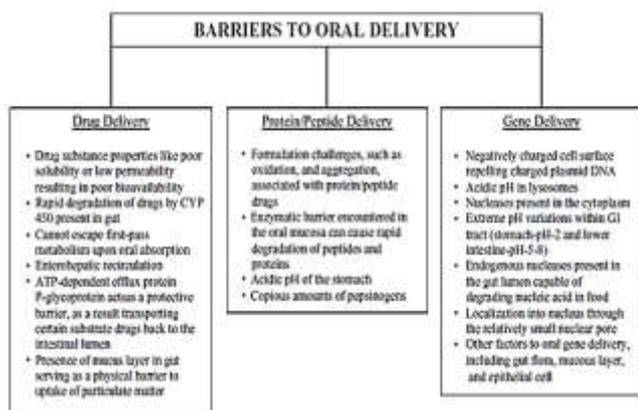


Figure 1 Barriers to oral delivery of drugs, protein/peptides, and genes.

IV. TECHNOLOGIES DEVELOPING FOR DRUG DELIVERY

Current research and development of drug delivery systems can be broken down into the following four general categories:

a. Routes of delivery

There are a variety of ways to take medications: by mouth, by absorption through the skin, by inhalation, or by intravenous injection. There are advantages and disadvantages to each method, and not all methods are available for every medication. One major research area therefore focuses on improving current delivery methods or creating new ones in order to enhance the use and performance of existing medications.

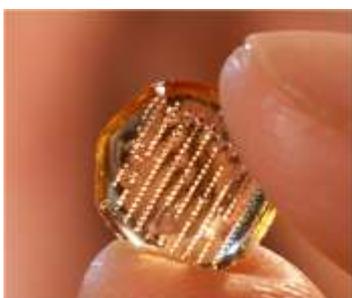


Figure 2 Image of microneedle patch the size of a fingertip used to deliver influenza vaccines. Photo Credit: Dr. Mark Prausnitz, Georgia Institute of Technology

For example, microneedle arrays are a new method, currently in development, for the delivery of medications through the skin. These arrays are made up of dozens of microscopic needles (each one much thinner than a human hair) that can either be coated or filled with medicine. The needles penetrate the skin easily, but because they are so

small, they don't touch any nerves, and so the delivery of the medication becomes a painless procedure.

b. Delivery vehicles

Ensuring that medications arrive at their destinations intact is the focus of this research area, which concentrates on finding the most suitable carrier for medications (just as the most suitable carrier for a drink of water, for example, is a glass rather than a plate).

One such cancer-treating carrier developed by researchers funded by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) is known as a "nanosponge." This delivery vehicle is essentially a scaffold built of tiny, specialized polyester particles that have been coated with disease-targeting compounds; the structure is then filled with an anticancer drug. Once they are injected into the body, the nanosponges move toward the tumors if targeted by antibodies to their intended site, and they undergo a safe and slow degradation process that releases the medication at a steady, controlled rate at the tumor site.

c. Cargo

Drug delivery researchers are presently expanding the scope of possible treatment options beyond conventional medications, exploring how genes, proteins, and stem cells might be used as treatments. For example, the NIBIB is currently working on a project to treat autoimmune disorders using protein treatments.

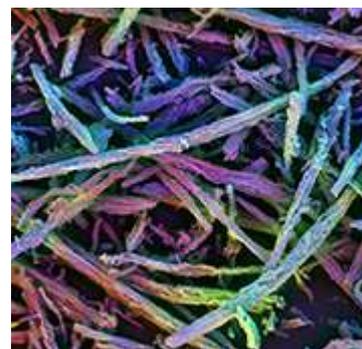


Figure 3 Polychromatic scanning electron microscopy of 3D vaccine consisting of microsized, porous silica rods. Source: James C. Weaver, Wyss Institute

Previously, the challenge with autoimmune diseases has been that most treatments rely on drugs that reduce the immune system's overall activity, thus increasing the risk of infection and other illnesses. In an attempt to avoid this, researchers are taking cues from the way the body naturally prevents an immune reaction, and are developing microscopic, biodegradable particles that have the ability to selectively shut down those immune cells associated with a particular autoimmune disorder, in this case multiple sclerosis.

d. Targeting strategies

Some aspects of drug delivery research start at the end and work backwards in the hope of finding a solution; in

other words, researchers start by examining a delivery method that already has a known target, such as an organ, a tissue type, or a disease-specific structure.

For example, NIBIB-funded researchers have developed a plant virus nanoparticle that has the ability to target and attach to prostate cancer cells. These viral nanoparticles take advantage of the ways in which viruses have naturally developed to overcome immune defenses and enter cells. This strategy brings a double benefit to researchers: the behavior and actions of the viral nanoparticles within the human body are already well understood, and they do not need as much modification as other nanoparticle types to behave in desired ways.

V. IMPORTANT AREAS IN TARGETED DRUG DELIVERY SYSTEMS

Advanced intravitreal drug delivery systems and devices

Ideally, liberation of the ophthalmic drugs from the DDS/delivery device in the posterior segment of the eye should be performed as sustained/controlled-release or even on-demand by an external stimuli. Most of these sustained-release DDSs are injected intravitreally once without any further needs for repeated injections, while some of the intravitreal devices such as micropumps are refillable systems. Of these, the nanoscaled biodegradable DDSs and sol-gel injectable hydrogels are novel effective ophthalmologic formulations that are deemed to provide maximal clinical benefits with minimal side effects. So far a number of advanced DDSs and devices has significantly improved the intravitreal drug delivery and targeting. Among them, smart NSs were shown to be able to efficiently circumvent the related barriers, enter into the posterior segment of the eye and pose minimal adverse Fig. 4.

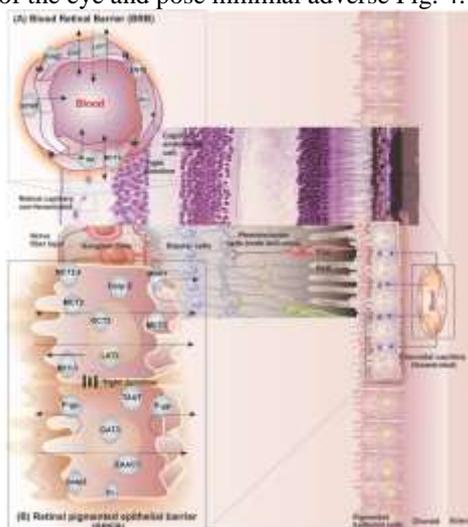


Figure 4 The retinal cellular structure. A) The inner blood retinal endothelial cells (RECs) form the blood-retinal barrier (BRB). B) The outer pigmented epithelial cells (PECs) form the retinal pigmented epithelial barrier (PREB). As polarized cells, both retinal endothelial and pigmented epithelial cells possess tight junctions and traverse of nutrients are selectively controlled by transport machineries as carrier-mediated transportation and receptor-mediated transportation.

The retinal cellular structure. A) The inner blood retinal endothelial cells (RECs) form the blood-retinal barrier (BRB). B) The outer pigmented epithelial cells (PECs) form the retinal pigmented epithelial barrier (PREB). As polarized cells, both retinal endothelial and pigmented epithelial cells possess tight junctions and traverse of nutrients are selectively controlled by transport machineries as carrier-mediated transportation and receptor-mediated transportation.95 Selected advanced DDSs and devices used to deliver ocular drugs into the posterior segment of the eye are shown in Fig. 5.

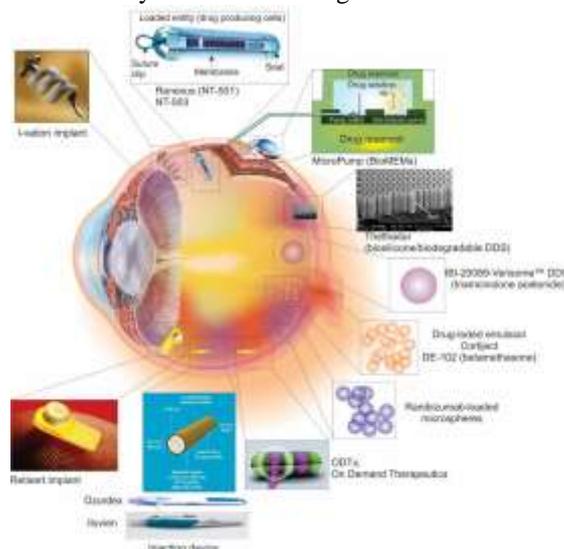


Figure 5 Advanced intravitreal drug delivery systems and devices

Biocompatible nanostructures for use in gene delivery developed by KAUST researchers

A tiny therapeutic delivery system that can control the body's ability to manufacture proteins has been developed by Saudi Arabia's King Abdullah University of Science and Technology (KAUST) researchers.

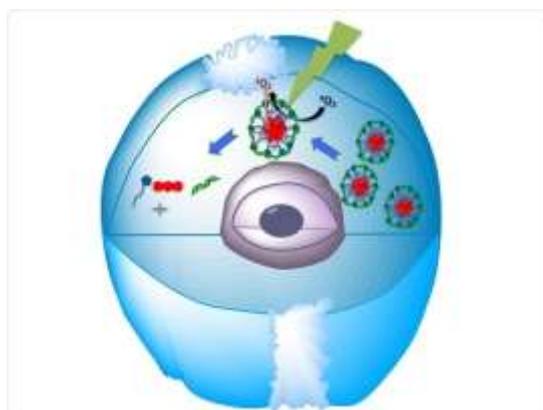


Figure 6 The self-assembled biocompatible nanomaterial delivers the miRNA into the cell and then releases it when struck by light. © 2016 KAUST

Khashab and her colleagues have now demonstrated biocompatible nanostructures for delivering siRNA and efficiently silencing genes¹. They combined the macromolecule histidine-capped-9,10-dialkoxy-anthracene (HDA) and siRNA in water. They observed the self-

assembly of spherical nanoparticles when the water was slightly acidic, but not when it was pH neutral.

Drug-loaded nanocarriers in tumor targeted drug delivery

Current cancer therapy approaches are based in surgery, radiotherapy and chemotherapy, being the chemotherapy the one that shows the greater efficiency for cancer treatment, mainly in more advanced stages. A major problem with this conventional chemotherapy is its toxicity and it also destroys healthy tissues resulting in systemic toxicity besides beneficial characteristics of killing cancer cells. Anticancer drugs also destroy healthy tissues resulting in systemic toxicity.

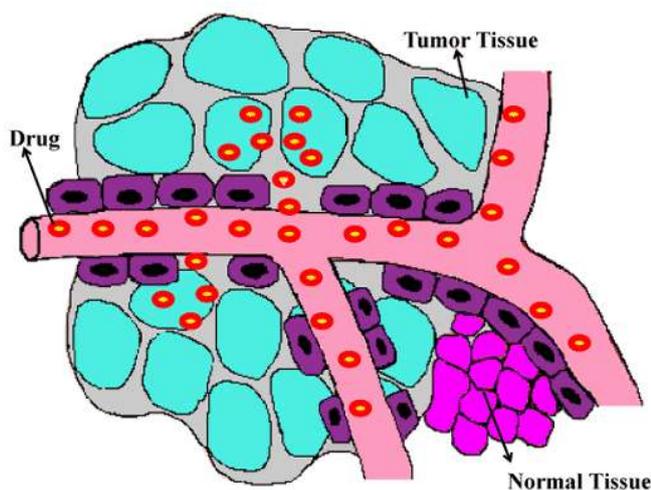


Figure 8 Nanoparticulate delivery systems in cancer therapies provide better penetration of therapeutic and diagnostic substances with the cancerous tissue in comparison to conventional cancer therapies. Credit: Dr. Buddolla Viswanath, Bentham Science Publishers

A possible solution to avoid these adverse influences is targeted drug delivery, which is a safer mode of delivering the medication at the desired site of its action in increased concentrations compared to other sites for maximal beneficial effect. The extremely small size of nanoparticles makes it advantageous and potentially superior to use for targeted drug delivery. In addition, these nanoparticle platforms allow for selective targeting of cancer cells or tumor vessels either by incorporating novel or standard anticancer drugs and/or the delivery of therapeutic genetic modulators.

VI. FUTURE RESEARCH IN TARGETED 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 the immune system defends the body against disease, each cell also has internal processes to recognize and get rid of potentially harmful substances and foreign objects. These foreign agents 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.

Combining Diagnosis and Treatment

The full potential of drug delivery systems extends beyond treatment. By using advanced imaging technologies with targeted delivery, doctors may someday be able to diagnose and treat diseases in one step, a new strategy called *theranostics*.

VII. CONCLUSION

Compared with traditional nanocarriers, the advantages of nanocrystals in physical stability, high drug loading and relative ease of production bring attractive alternatives for delivery of poorly soluble drugs. Both top-down and bottom-up techniques have been developed for preparing nanocrystals. The bottom-up techniques may be more suitable to prepare nanocrystals for i.v. injection than the top-down techniques, considering the potential contamination from milling media.

REFERENCES

- [1] B Eaton, "A Look at the Future of Drug Delivery Systems", May 27, 2016.
- [2] Drug Delivery Systems: Getting Drugs to Their Targets in a Controlled Manner, available at <https://www.nibib.nih.gov/science-education/science-topics/drug-delivery-systems-getting-drugs-their-targets-controlled-manner>
- [3] Edible ginger-derived nano-lipids could effectively deliver drugs for treating colon cancer", September 6, 2016 available at <http://www.news-medical.net/news/20160906/Edible-ginger->

[derived-nano-lipids-could-effectively-deliver-drugs-for-treating-colon-cancer.aspx](#)

- [4] Barar J., et al, "Advanced drug delivery and targeting technologies for the ocular diseases", *BioImpacts*, 2016, 6(1), 49-67.
- [5] Meerza Razak et al. Drug-Loaded Nanocarriers in Tumor Targeted Drug Delivery, *Current Biotechnology* (2015)