What if new drug delivery methods revolutionised medicine?

Nanoparticles lie at the heart of a new method for delivering medicines inside the body – and they were crucial to the success of the Covid-19 mRNA vaccines. This new drug delivery method and others could transform the way we treat disease, potentially boosting the treatment of Alzheimer's, Parkinson's and HIV, among others. Insulin and Covid-19 vaccines might even become available as pills. Can the European Union stay on top of this trend? And what challenges lie ahead?

Developing a vaccine usually takes more than 10 years. But when the Covid-19 pandemic hit, vaccines were rolled out at an unprecedented speed. China notified the WHO of a cluster of cases of pneumonia on 31 December 2019. Less than one year later, the EU regulator approved the BioNTech-Pfizer mRNA vaccine. Moderna's version – another mRNA vaccine – followed two weeks later.

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First proposed in the 1990s, medical use of mRNA vaccines was only made possible by recent advances in drug delivery. These vaccines contain a set of 'instructions' (mRNA) that tell cells how to produce viral proteins, which then trigger an immune response. Getting highly delicate mRNA into cells is far from easy, however. To protect the mRNA and facilitate its delivery, scientists encapsulated it in tiny lipid nanoparticles; without these, the BioNTech-Pfizer and Moderna vaccines would not exist.

These mRNA vaccines exemplify a crucial issue in drug development: finding effective drugs is only part of the task. Pharmacologists also need to find ways to deliver them to the parts of the body where they are needed. Tablets and capsules are easy and convenient, but many drugs (such as insulin) degrade rapidly in the gastrointestinal tract. These drugs are administered by injection, an unpleasant method with poor patient compliance. In addition, therapeutic agents in pills and injections are transported by the circulatory system, and often reach the whole body. This increases the risk of side-effects. Many otherwise effective drugs are discarded on account of their unacceptable side effects. Designing these drugs to reach only their intended site of action could unleash their potential.

Until the Covid-19 pandemic, drug delivery had not witnessed a breakthrough for a few decades. That could be about to change. Nanotechnology, new materials and novel devices promise to revolutionise the field.

Potential impacts and developments

Drug delivery refers to methods and devices for transporting medicines to their targets inside the body. The ideal drug delivery method releases the ingredient exactly where it is needed: to the whole body or targeted at certain sites. It also controls the rate and time of release – sometimes extending over long periods of time.

Implantable devices can release drugs at a defined rate for weeks or even months. They also offer targeted delivery, thereby reducing the risk of side effects. Implantable devices have been used in contraception and cancer treatment, but their potential is much wider. US researchers have developed an implantable capsule that uses thousands of nanochannels to control the drug release rate, and could be used to treat HIV for a year. Coupled with 3D printing, implantable devices could be personalised further to meet individual patients' needs.

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The delivery of drugs to the brain is a major challenge in drug development. The blood-brain barrier (BBB), which consists primarily of closely wedged endothelial cells lining the interior of the capillaries that connect the bloodstream to brain tissue, prevents toxins and pathogens from reaching the brain. It is also impenetrable for many drugs. Yet delivering drugs past the BBB is crucial to treating neurodegenerative diseases, such as Parkinson's and Alzheimer's. Focused ultrasounds can be used to disrupt the BBB temporarily; this method can be enhanced through combination with the intravenous administration of microbubbles. Electric pulses can also be used to create micro-and nanopores to allow therapeutic ingredients to pass to the brain. Alternatively, the nasal route can be used to bypass the blood-brain barrier.

About 60 million Europeans have diabetes and many of them require regular insulin injections. Developing oral forms of insulin would significantly improve their quality of life and enhance patient compliance. Unfortunately, insulin and similar drugs (biologics, i.e. substances consisting of a living organism or its products) are highly susceptible to degradation in the gastrointestinal tract. Furthermore, unlike most oral medications, these are big molecules that are not easily absorbed by the intestine. To overcome these barriers, pharmacologists are seeking to improve biologics' stability. They are also working on coatings to protect the drug cargo, and permeation enhancers to temporarily increase permeability across the intestine. On this note, some researchers claim that the next Covid-19 vaccine could be taken as a pill.

Nanomedicine is often seen as the technology destined to revolutionise drug delivery. Nanoparticles smaller than 100 nanometres (1 000 times smaller than a human hair) could soon make it possible to reach targets previously considered 'undruggable'. They could also combine diagnostics and medical treatment in a single drug (theranostics), and help break the BBB.

However, nanoparticles have faced increased criticism in recent years. Promising results on mice in the 1990s persuaded researchers that a breakthrough in cancer treatment was easily within reach and public bodies devoted significant funding to it. Two decades later, that promise has yet to materialise. Cancer treatment still relies mainly on radiotherapy and chemotherapy. In 2018, only 34 nanomedicines were approved in the EU. Some researchers openly questioned whether nanoparticles would ever deliver, and highlighted the risk of overfunding this research at the expense of other promising technologies.

In the end, nanoparticles were vindicated, not by a breakthrough in cancer therapy – but by the overwhelming success of mRNA vaccines. There are hopes that this success will precede many others. The sequencing of the human genome has enabled the development of large numbers of drugs based on peptides and proteins. Delivering these molecules will be more challenging than delivering conventional drugs, and nanoparticles could be the enabling technology to make this happen. Nanoparticles could also be crucial in gene therapy.

Anticipatory policy-making

In 2020, the global market for advanced drug delivery systems amounted to US$231 billion, and this figure is expected to rise to US$310 billion by 2025. The EU is second to the US in the global pharmaceutical market, and access to quality healthcare is the third most pressing concern of European citizens. Technological advances could soon transform traditional drug delivery, and proactive policy-making could help the EU stay on top of these developments. The European Commission and EU Member States invested heavily in research on nanoparticles, which were ultimately crucial for mRNA vaccines. Nevertheless, to date, nanoparticles have not delivered in the area where they were most promising: cancer therapy. Additional research and efforts are needed in this regard.

The advent of cheaper, safer and more effective ways to deliver gene therapy could boost 'biohacking' and transhumanism. Although governments do have legal tools to curb practices that endanger public health and several EU Member States ban genome editing outside licensed laboratories, emerging technologies could fall in legal grey zones, raising new ethical dilemmas, and making government oversight even more difficult. These are the challenges that policy-makers could be facing shortly; evidence-informed foresight and preparedness are key to providing effective responses.

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