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Brewing nucleic acid therapies at the point of care

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A Viewpoint on the Frontiers in Science Lead Article

NANOSPRESSO: toward personalized, locally produced nucleic acid nanomedicines

Key points

- Nucleic acid-based medicines have revolutionized disease treatment, with lipid nanoparticles (LNPs) playing a key role in delivering them into cells. However, robust and accessible delivery solutions for many conditions are lacking.
- NANOSPRESSO proposes the on-site production of LNP formulations of RNA drugs to fit each patient's specific needs, analogous to coffee capsules tailored to individual tastes—providing efficient, accessible, high-quality delivery, even by non-experts.
- Implementing these models will require resources that ensure sterility and good manufacturing practice (GMP) compliance, suitable regulatory and legal frameworks, and measures to safeguard supply chains and data.

Introduction

A small capsule, a push of a button, and moments later, a perfect cup of coffee. The simplicity and reliability of capsule coffee machines have reshaped how we experience a process that was once artisanal and variable. What if the future of personalized medicine were just as accessible? In their lead article, Estapé Senti et al. drew inspiration from coffee capsules to develop the NANOSPRESSO concept for on-demand production of personalized nucleic acid therapeutics by leveraging automated microfluidic cartridges loaded with customized nucleic acid formulations (1).

RNA drugs, such as antisense oligonucleotides (ASOs), small interfering RNA (siRNA) and messenger RNA (mRNA), are ideal therapeutic payloads for the NANOSPRESSO system because they enable the regulation of gene expression in a programmable and transient manner. ASO and siRNA therapeutics can silence harmful genes, which is especially useful

for diseases driven by overactive or mutated genes (2). mRNA therapies work by instructing cells to produce specific proteins, making them suitable for applications such as protein replacement, cancer immunotherapy, and vaccination (3). These molecules can be rapidly synthesized and customized for individual patients, allowing for fast, sequence-specific responses to rare mutations or emerging diseases. Their synthetic nature, safety profiles, and proven clinical potential make them well-suited for decentralized, small-batch manufacturing within automated NANOSPRESSO systems.

Lipid nanoparticles (LNPs) are the delivery system of choice due to their high efficiency in encapsulating RNA molecules (4). These nanoparticles can also protect RNA molecules from enzymatic degradation, and facilitate cellular uptake and endosomal escape to promote cytosolic functions. Moreover, LNPs can be precisely formulated using microfluidic systems (5), which are ideal for the automated production of NANOSPRESSO. The modular composition of LNPs also allows for the tuning of properties such as size, surface charge, and biodistribution (6), supporting tailored formulations for specific disease targets and the overcoming of biological barriers (7). Because LNPs have already been proven effective in humans through their use in mRNA vaccines, they also provide regulatory and translational advantages.

NANOSPRESSO would lower the barriers to translation by enabling bedside fabrication in hospitals and clinics through a sterilized and automated process, eliminating the need for traditional pharmaceutical infrastructure. Thus, the model has the potential to open the door to affordable therapies, particularly for orphan diseases that are often neglected due to the associated limited market size and the high costs of individualized drug development. In doing so, NANOSPRESSO could accelerate the transition from diagnosis to treatment, potentially reducing timelines from months to days.

Implementation landscape

By harnessing automated microfluidic systems, NANOSPRESSO could bring precision manufacturing directly to hospitals. Several commercial microfluidic devices that use disposable cartridges are available for precise nanoparticle assembly. Moreover, self-powered, microfluidic modules that support milliliter-scale flow rates, could be adapted for nanoparticle manufacturing, avoiding the need for external pumps or equipment (8). To optimize nanoparticle assembly, the microfluidic chips should be standardized for efficient mixing of components by controlling their geometry, materials, and flow paths (5). Thus, these chips could embody the “one-button” reliability of coffee pods, while meeting pharmaceutical-grade requirements.

Digital formulation engines could be integrated into the hardware, translating patients’ multiomic and clinical data into a precise mix of nucleic acids, lipids, polymers, and flow parameters. The machine could then program the flow rates and mixing sequences to produce tailored vehicles. Furthermore, advances in LNP design driven by artificial intelligence (AI) could predict the optimal nanoparticle composition based on extensive datasets of material properties and biological responses (9).

As these innovations unfold, regulatory bodies are evolving to accommodate the automated, decentralized compounding of advanced therapies. New good manufacturing practice (GMP) guidelines now permit these practices, marking a significant shift in how therapies are developed and administered. In this context, NANOSPRESSO may bypass traditional manufacturing lead times with on site manufacturing. For example, a case study on decentralized three dimensional–printed drug manufacturing demonstrated that small-batch, onsite production can meet stringent quality metrics in less time (10). Importantly, quality control is also being re-engineered on chips. Thus, microfluidic quality control modules could be miniaturized for particle size analysis, encapsulation-efficiency assays, and sterility checks of each batch, replacing bulky chromatography techniques and electron-microscopy workflows. In addition, quality control results can be stored automatically for regulatory traceability.

As software, materials and regulatory frameworks converge, a clear path is emerging for on-demand, personalized nucleic acid drugs to become a routine clinical practice rather than a global manufacturing challenge.

The road ahead

Although the NANOSPRESSO platform is a groundbreaking concept, several challenges may threaten its implementation. One of the most pressing concerns is maintaining sterility and GMP compliance at the point of care. Unlike controlled manufacturing facilities, ensuring aseptic conditions in hospitals is complex, expensive, and prone to human error. Thus, implementing appropriate controls, monitoring systems, and staff training is crucial for the progress of this technology. These points must be carefully planned, as they may require significant investments that could exceed the cost-saving premise of the approach.

While regulations are beginning to address point-of-care drug manufacturing, the regulatory and legal framework for the NANOSPRESSO approach remains largely undefined. Agencies may demand extensive validation protocols, rigorous quality controls, and comprehensive documentation systems, which could hinder the platform’s speed advantages. Moreover, these requirements may vary widely between countries. At the same time, the model may introduce significant liability uncertainties, making it essential to clearly define the responsibilities of hospitals, machine and cartridge manufacturers, drug developers, and software providers in order to navigate these complexities effectively. Importantly, without a robust accountability framework, healthcare institutions may view the adoption of this technology as an increased risk, regardless of its clinical potential. This is especially critical because, in the event of an early failure, there is a risk that the entire NANOSPRESSO approach could be abandoned. Thus, a well-defined framework that clearly assigns roles and responsibilities would not only help mitigate this risk but

also enable the precise identification and correction of issues, ensuring the long-term viability of the platform.

While NANOSPRESSO would also reduce industrial-scale costs, expenditures arising from single-use cartridges, microfluidic devices, maintenance, quality assurance, and staff training could still be prohibitive for many hospitals. However, it should be noted that cost saving is not the primary goal of the NANOSPRESSO approach. Rather, the main benefit lies in enabling the efficient and accessible treatment of diseases, regardless of whether cost reduction is achieved. Moreover, despite its decentralized design, NANOSPRESSO may remain reliant on centralized supply chains. In particular, critical components such as pharmaceutical-grade RNA oligonucleotides, specialized ionizable lipids, and optimized cartridges would probably be produced by only a limited number of suppliers, suggesting that any upstream disruption in the supply chain could halt treatments. NANOSPRESSO may also face digital vulnerabilities, as automated software, secure firmware, and cloud-based updates may introduce cybersecurity risks and hospital information technology compatibility challenges. Although these issues can often be mitigated, for example, by using a secure, offline computer interface or establishing a robust and encrypted connection, they should be carefully considered to maintain production and safeguard patient data.

Conclusion

The NANOSPRESSO system has high potential to enable the point-of-care production of nucleic acid-loaded LNPs, bypassing the logistical and scalability limitations of centralized manufacturing. Its validated microfluidic cartridges, integrated quality control, and consistent nanoparticle formation demonstrate its readiness for clinical integration. Unlike conventional LNP platforms, NANOSPRESSO offers modularity for other nanoparticle technologies, such as polyplexes and polymeric micelles, potentially enabling differential targeting strategies. This versatility could shift genetic medicine from industrial bottlenecks to bedside application through flexible formulation and faster paths to treatment.

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HC: Writing – original draft, Writing – review & editing, Conceptualization.

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