

Q&A with Ardena Experts

Microfluidization for Precision Nanoparticle Engineering

Ali Dadfar, PhD,
Senior Scientist - Nanomedicine Process Research and Development

What is a microfluidizer, and what is its role in nanoparticle production?

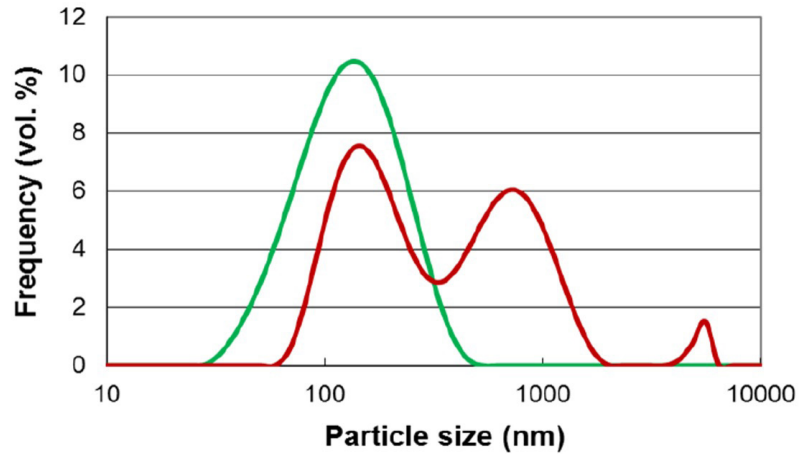
A microfluidizer is a high-pressure processing device that utilizes interaction chambers with a fixed geometry to generate intense shear forces. In nanoparticle production, this process facilitates the size reduction and uniform dispersion of materials. For example, in the production of liposomes and lipid nanoparticles (LNPs), microfluidization reduces the size of lipid structures, enabling them to self-assemble into vesicles with the desired size and lamellarity. Microfluidizers also find applications in nanoemulsion production, cell disruption, polymer nanoparticle synthesis, and particle size reduction.



▲ Microfluidization Technology: A Powerful Tool for Achieving Controlled Particle Size and Enhanced Product Stability Through High-Shear Processing

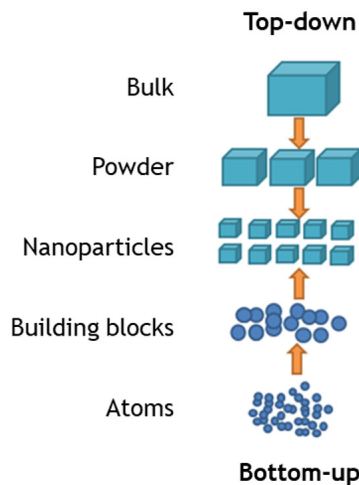
What are the primary applications of the microfluidizer in Ardena’s Nanomedicines business unit?

In Ardena’s Nanomedicine group, the primary potential applications of the microfluidizer include the downsizing of nanoparticles and large molecules, to achieve uniform size and improve their characteristics for drug delivery.



How does microfluidization differ from other nanoparticle synthesis techniques used at Ardena?

While Ardena focuses on “bottom-up” nanoparticle synthesis, the microfluidizer is a “top-down” technique. As an example, it doesn’t create liposomes from scratch but reduces the size of pre-formed lipid structures. This contrasts with bottom-up methods that use other methods to form vesicles. Other methods like extrusion or microfluidic chips are also used, but microfluidization offers advantages in scalability, speed, and concentration.



What are the key advantages of using a microfluidizer for nanoparticles production like liposome compared to other methods?

Key advantages include the production of high-quality liposomes with uniform and small particle size, the ability to generate high concentrations of liposomes directly, fast processing times, inherent scalability for production, solvent independence, temperature control, and flexibility in producing different liposome sizes and formulations.

How does the microfluidizer ensure the production of high-quality nanoparticles?

The microfluidizer produces uniform shear through its fixed-geometry interaction chamber and constant pressure pumping system. This effectively creates uniform nanoparticles (e.g. Liposome) with a narrow particle size distribution, ensuring high quality.

Can the microfluidizer produce liposomes at therapeutic concentrations directly? If so, how?

Yes, the microfluidizer can produce liposome solutions at therapeutic concentrations directly. It can achieve lipid concentrations well within the range of ready-to-be-administered liposomal drugs and even higher, eliminating the need for downstream concentration processes.

How does microfluidization affect the size and lamellarity of liposomes and LNP?

Microfluidization, as a top-down method, reduces the size of pre-formed lipid structures, allowing them to self-assemble into vesicles with the desired size and lamellarity. It's a size reduction process rather than a vesicle formation process itself.

Is the microfluidizer suitable for encapsulating sensitive active ingredients, such as biologics (DNA/RNA, proteins)?

While the high shear rates could potentially impact sensitive biologics, the microfluidizer has been successfully used in cell disruption without causing damage. Additionally, temperature control is effective, and many liposomal drugs involve small molecules that are stable under microfluidization conditions. Larger proteins such as ovalbumin can also withstand higher levels of stress/shear.

Is microfluidizer technology scalable for large-scale pharmaceutical manufacturing of nanoparticles?

Yes, microfluidizer technology is inherently scalable. It can produce therapeutic concentrations at any scale, from lab-scale (liters per 10 minutes) to production-scale (hundreds of liters per hour or thousands of liters).

How does the scalability of microfluidization compare to other nanoparticle production methods?

Many alternative methods, such as microfluidic chip methods, are not easily scalable and often produce dilute concentrations requiring downstream processing. Microfluidization is superior in its ability to maintain product quality and concentration across different scales.

How does microfluidization contribute to efficient production processes?

Microfluidization leads to very fast size reduction of liposome or LNP vesicles, resulting in short process times, especially when compared to slower processes like extrusion or microfluidic chip techniques.

Does the microfluidizer require the use of solvents during the size reduction process?

Generally, the microfluidizer size reduction process does not require solvents, eliminating the need for solvent removal. However, it is compatible with commonly used solvents if the formulation process requires them.

Can the microfluidizer be used to produce different sizes and types of nanoparticles?

Yes, the microfluidizer is flexible. Microfluidizer can be used for nanoemulsion production, cell disruption, polymer nanoparticles, liposomes, LNP, particle size reduction, molecular weight reduction.

Is it possible to filter liposomes produced using microfluidizer technology and can this device be qualified for GMP production?

Yes, studies confirm that liposomes produced using a microfluidizer processor can be successfully filtered through a 200nm filter for sterile filtration and the device can be used for GMP production.

Can the microfluidizer be used for applications beyond liposomes and LNPs, such as nanoemulsions and polymer nanoparticles?

Yes, microfluidizer technology is also well-suited for creating nanoemulsions for insoluble drug delivery and for the production of polymer nanoparticles, including solid lipid nanoparticles (SLNs).

What advantages does microfluidization offer in the production of nanoemulsions?

Microfluidization offers the production of extremely small droplets with a narrow particle size distribution, improving stability and filtration. It is also easy to operate, scale up, and reliable, with capacities ranging from 2ml to liters per hour.

**Navigating you
through drug development**