PROCESS DEVELOPMENT OF A DRUG DELIVERY LIPOSOME AND POST PROCESS FILTRATION WITH 0.2 MICRON RATED FILTERS

BY: K. JANDRASITZ, S. MESITE AND Y. SU, MICROFLUIDICS INTERNATIONAL CORPORATION, WESTWOOD, MA, USA

R. TURMELL, K. MARINO AND M. FOLMSBEE, PALL LIFE SCIENCES, PORT WASHINGTON, NY, USA

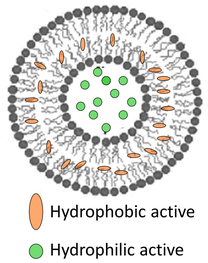
INTRODUCTION

Nanomaterial Drug Delivery Systems

- Effective delivery by overcoming the transport barriers.
- Engineered materials to target specific cells.
- Increased bioavailability at reduced drug load.
- Reduced systemic side effects.
- Controlled release capabilities.

Liposomes

- Spherical lipid vesicles with bi-layered membrane structure.
- Can encapsulate either hydrophilic or hydrophobic actives, or both.
- One of the most successful and clinically established drug delivery systems.

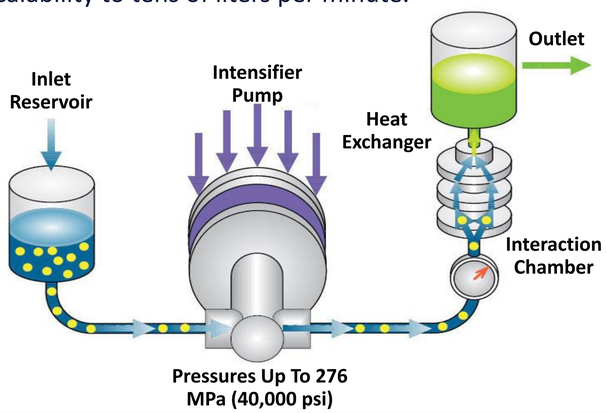


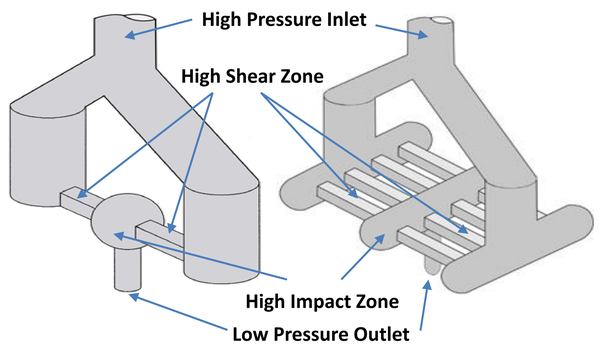
Key Production Requirements & Challenges

- Process efficiency.
- Sterile production.
- Repeatability & scalability.
- cGMP/21 CFR 11 compliance.

MICROFLUIDIZER® TECHNOLOGY

- High pressure is used to pump multi-phase fluids through the microchannels of an interaction chamber.
- Velocities of over 400 m/s in micro-channels result in shear rates of up to 10^8 s-1.
- Parallel arrays of identical micro-channels ensure linear scalability to tens of liters per minute.





METHODS

Materials

- Liposome was formulated by dispersing 5% wt. soybean oil and 1.5% wt. Lipoid S100 in aqueous phase.

Liposome Preparation & Particle Size Analysis

- The mixture was shear mixed using a rotor-stator mixer first and then processed with a M-110EH Microfluidizer®.
- Parameters varied during processing: pressure and number of passes through the processor.
- Particle size analyzed using a laser diffraction particle size analyzer (Horiba LA950).

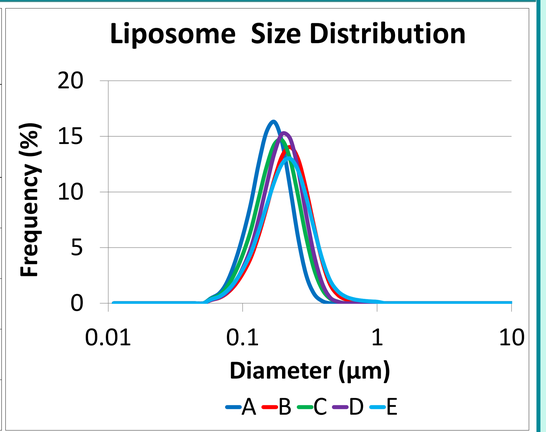
Post-process Filtration

- All samples were passed through 0.2–micron rated filters.
- Filter materials used:
  - ❖ Fluorodyne® II DFL – Dual layer PVDF membrane
  - ❖ Fluorodyne EX EDF – PES membrane over PVDF membrane
  - ❖ Supor® EKV – Dual layer PES membrane
  - ❖ Supor EX ECV – Dual layer PES membrane
- All filters were manufactured by Pall Life Sciences.

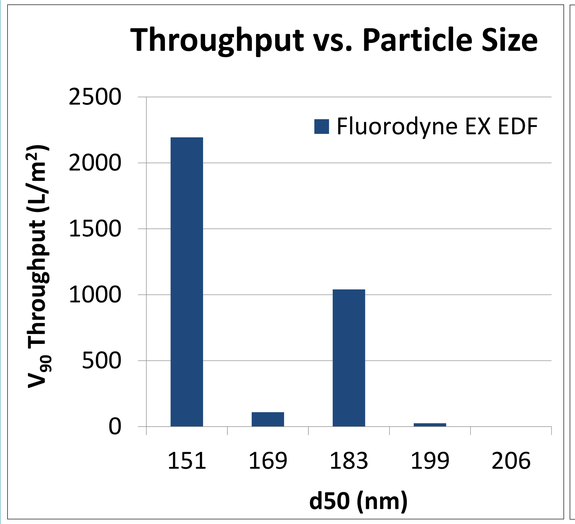
MICROFLUIDIZER RESULTS

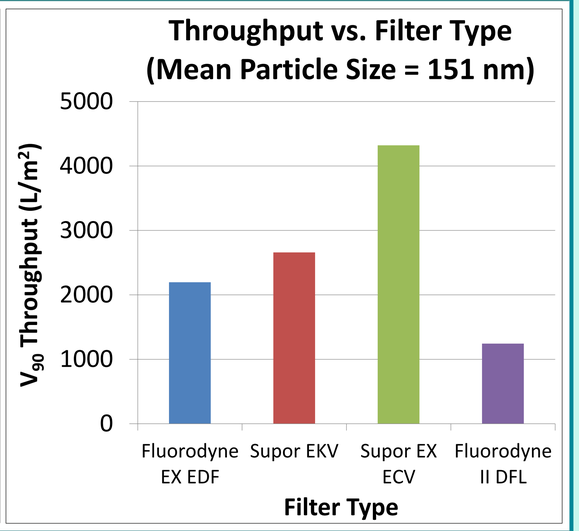
Particle Size Measurements

Test	Pressure (psi)	# of Pass	d10 (nm)	d50 (nm)	d90 (nm)	d95 (nm)
A	20,000	2	94.0	150.9	224.3	299.8
B	20,000	1	114.6	199.2	319.4	468.2
C	25,000	1	100.9	169.0	264.4	372.0
D	8,000	1	109.4	183.0	281.0	379.4
E	30,000	1	113.6	206.3	351.1	645.2



FILTRATION RESULTS





CONCLUSION

- A high shear Microfluidizer® processor was used to develop a drug delivery liposome.
- Liposome particle size and size distribution can be precisely controlled by adjusting process conditions.
- Filtration throughput depends on particle size and size distribution. The highest filtration throughput was achieved with the smallest mean particle size of 151nm.
- Filter membrane materials also affect filtration throughput. All filters tested in this study demonstrated robustness for samples with mean particle size of 151nm.
- Bacteria challenge test results pending. All results shown are throughput at size range only and do not indicate bacterial retention or product recovery.