

## Manufacturing of sterile liposomes with high entrapping efficiencies

Liposomes are innovative drug-carriers which allow the efficient transport of active pharmaceutical substances (e.g. cytostatics, nucleic acids, proteins or peptides) into cells, organs or tumors. Actual methods for manufacturing liposomes are time-consuming and labor-intensive and encapsulation efficiencies are mostly low.

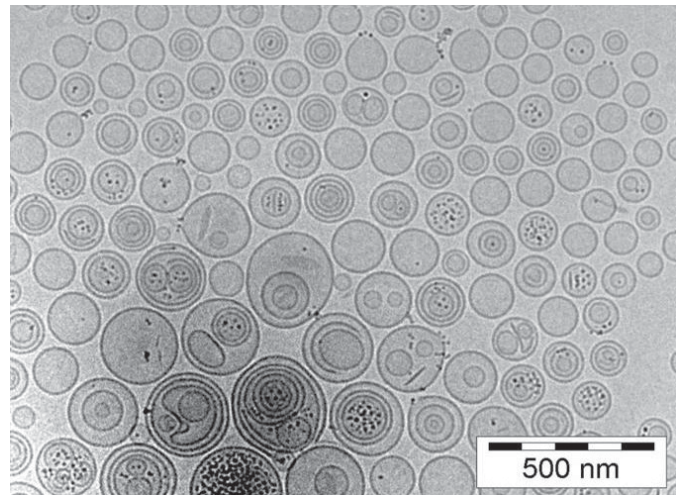
„In-vial-homogenization” of lipids and active ingredients by using the new ZentriMix 380 R allows the easy and fast production of sterile liposomes with high entrapping efficiencies.

In contrast to other liposome manufacturing techniques, batch sizes can be very small, what is an advantage if only minor amounts of active ingredients are available (e.g. siRNA, antibodies). However, these small batches are fully comparable to bigger batches which can be produced by using the ZentriMix 380 R as well.

Since liposome manufacturing using the ZentriMix 380 R is a fast and sterile process, the preparation of liposomes with limited shelf lives for immediate use is possible as well. This principally allows the investigation of „per-se” instable but promising liposomes and – in a later step – its clinical investigation and use (bed-side-preparation).



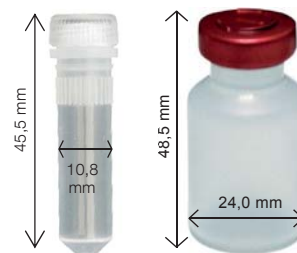
ZentriMix 380 R



Electron micrograph of liposomes loaded with iron oxide particles

### Advantages of manufacturing liposomes by using the ZentriMix 380R

- High entrapping efficiencies.
- Sterile, safe and easy.
- Gentle procedure, suitable for using sensitive drugs or lipids.
- Milligram to gram batches by using the same technique.
- Just-in-time manufacturing (investigation of non-stable liposomes).
- Various liposome types: conventional-, stealth-, pH- or temperature-sensitive liposomes, immunoliposomes.



ZentriMix-vials for liposome production (2 ml & 10 ml)

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## Manufacturing of liposomes using the ZentriMix 380 R

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### 1. Select vial according to batch size :

- 100 – 600 mg: 2 ml ZentriMix-vial\* (I)
- 600 – 2,000 mg: 10 ml ZentriMix-injection vial (II)

### 2. (sterile) weighing

- lipid or lipid-mixture
- aqueous phase/buffer
- active substance (preferred dissolved in aqueous phase)
- mixing aid\*\*

### 3. In-vial homogenization using the ZentriMix 380 R

- rotation speed: 2,350 rpm
- temperature: 0 - 20°C
- time: 30 minutes
- samples: max. 40

### 4. Redisperse and use

\*sterile Screw Cap Micro Tube, 2 ml, PP from Sarstedt, Germany, ordering no. 72.693.005 suitable for our adapter 3236

\*\*0.6 g 1.5mm (I) resp. 3.5 g 1.1mm (II) Zirconoxide ceramic beads (stabilized with Yttriumoxide) (Sigmund Lindner GmbH, Warmensteinach, Germany)

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ZentriMix-Rotor carrying vial adapters for 2 ml Screw Cap Micro Tubes. Each rotation unit carries two adapters which lie on each other. Only the adapters on top are visible.

#### Example: Gemcitabine-Liposomen

- Lipid-mixture: DPPC/Cholesterol (55:45 mol%)
- Entrapping efficiency Gemcitabine:  $62.8 \pm 2.2 \%$
- Mean diameter:  $156 \pm 11 \text{ nm}$
- Polydispersity-index:  $0.15 \pm 0.06$

### Ordering information

	Ordering No.
ZentriMix 380 R, Dual Centrifuge, refrigerated, without rotor, 200-240 V 1~, 50-60 Hz	3200
ZentriMix 380 R, Dual Centrifuge, refrigerated, without rotor, 110-127 V 1~, 60 Hz	3200-01
S-rotor, 2-place, 2500 RPM, without Adapter	3205
Adapter(Set), 20-place, for conical 2 ml Sarstedt PP micro tubes with screw cap (Cat.No. 72.693.005), for rotor 3206,3205 Set of 2 pcs.	3236
Removal aid for adapter 3236	3210
Adapter(Set), 2-place, for 10 ml injection vial*, for rotor 3206,3205 Set of 2 pcs.	3211

\* Only use ISO 8362 injections vials made of polypropylene (no glass!). Together with the stopper and aluminum crimp seal, the vial should be 48.5 mm high to fit into the adapter.