Development of mesoporous silica nanoparticle-supported lipid bilayer as drug delivery systems

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Introduction

- Targeted drug delivery systems precisely treat cancer cells and minimise toxic effects on healthy cells compared to conventional chemotherapy treatment [1].
- Among these systems, Mesoporous silica nanoparticles (MSNs) offer high internal surface area and tuneable particle and pore sizes but suffer from poor biocompatibility [2].
- Whereas Liposomes are highly biocompatible but exhibit low structural stability and a tendency to leak encapsulated drugs[3].
- Research Objective: To develop a hybrid nanocarrier that integrates the structural benefits of MSNs with the biocompatibility of liposomes for advanced drug delivery.

Methods

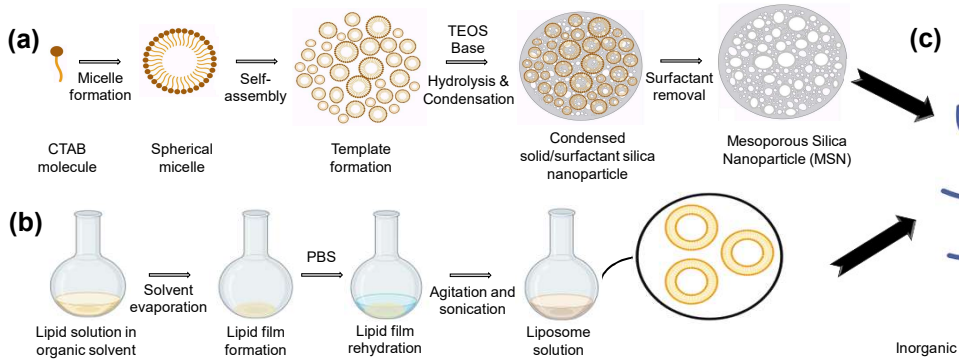

Table 1. Comparative Summary of MSN Synthesis Methods and Their Nomenclature. * reference in the results section

Base	Silica conc.	T(°C)	Sample Label
Sodium Hydroxide (2M)	TEOS	80°C	M100
Ammonium Hydroxide	0.8 M TEOS in EtOH	50°C	MMR
Diethanolamine	TEOS	95°C	MMO
Triethanolamine	TEOS	85°C	MIT
Sodium Hydroxide (0.1M)	0.8 M TEOS in MeOH	30°C	MCK

Fig 1. Protocell produced via (a) base-catalysed sol-gel silica formation, (b) lipid bilayer synthesis by thin film hydration, and (c) assembly through spontaneous membrane fusion.

Results

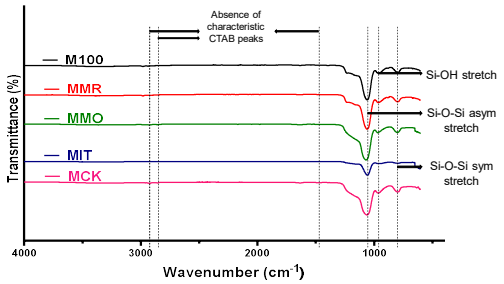

Fig 2. FTIR spectra of the synthesised MSNs after surfactant removal. The characteristic peaks within the nanoparticles were identified.

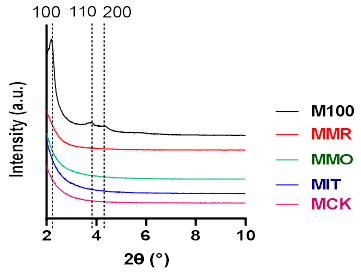

Fig 3. XRD pattern of the nanoparticles. The pore structure order of the MSNs was confirmed.

Table 2. Reported % CTAB concentration from TGA and nitrogen adsorption-desorption measurements for the MSNs. TGA confirmed the effective removal of CTAB indicated by the weight loss between 150 to 360 ºC. A characteristic type IV isotherm plot is recorded for all the MSN families.

MSN sample	% CTAB conc.	BET surface area (m^2/g)	Pore volume (cm^3/g)	Average pore diameter (nm)
M100	~3.0	936	0.89	2.6
MMR	~2.6	1,028	0.96	2.9
MMO	~2.6	739	0.71	3.0
MIT	~2.8	600	0.53	2.8
MCK	~5.1	122	0.10	3.0

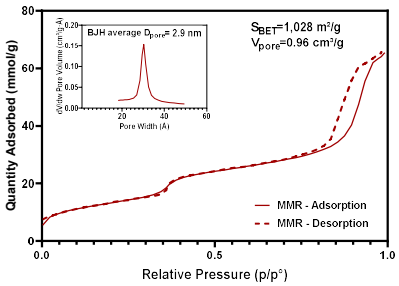

Fig 4. Nitrogen adsorption-desorption Isotherm Plot of MMR. A Type IV isotherm plot characteristic of a mesoporous material having a monomodal narrow pore size distribution was recorded.

Table 3. Reported DLS and zeta-potential measurements of the MSNs. The samples were dispersed in Milli-Q water and measured using a Malvern Zetasizer. *Data represented as **mean ± SD**, (n=3).

Sample	Dry Sample (SEM)	Sample in Dispersion (DLS)		
	Particle Diameter (nm)	Hydrodynamic Diameter (nm)	Polydispersity Index (PDI)	Zeta (ζ)-Potential (mV)
M100	85 ± 15	241 ± 13	0.3	-25± 1
MMR	40 ± 6	180 ± 1	0.3	-6 ± 1
MMO	52 ± 8	116 ± 4	0.3	-24 ± 1
MIT	50 ± 7	75 ± 1	0.1	-8 ± 1
MCK	81 ± 10	207 ± 1	0.2	-3 ± 1
LP_DSCP	-	90 ± 1	0.1	-2.9 ± 1
PC_MMR	-	143 ± 27	0.3	-3 ± 3

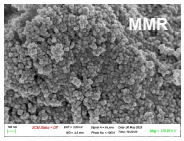

Fig 5. Characterization of MMR via SEM Imaging (135 KX mag.) The spherical morphology and uniform synthesis of MMR (Size: 40 ± 6 nm) was observed.

Table 4. Reported colloidal stability of MSN candidate (MMR) and Protocells (PC_MMR) over one month. Hydrodynamic diameter and PDI of samples dispersed in Milli-Q were measured initially and after one month of storage at 4 °C.
*Data represented as **mean ± SD**, (n=3).

Sample	Original		After 1 month, 4°C	
	Hydrodynamic diameter (nm)	PDI	Hydrodynamic diameter (nm)	PDI
MMR	180 ± 1	0.3	598 ± 129	0.4
PC_MMR	137 ± 11	0.3	121 ± 2	0.3

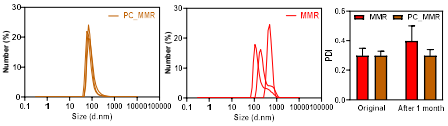

Fig 6. Recorded particle size distribution plot of samples after 1 month. The samples are dispersed in Milli-Q water.

Conclusion

- Diverse families of small-sized MSNs were successfully synthesised, coated with lipid bilayers, and characterised as protocell systems.
- A systematic investigation of MSN synthesis parameters and protocell drug loading efficiency is currently in progress.
- Future studies will focus on evaluating release kinetics and cellular biocompatibility of the protocells.

Acknowledgments

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References:

[1] Kashyap BK et al. ACS Omega 2023;8:14290–320.
[2] Florensa M et al. Pharmaceutics 2022;14:2703.
[3] Butler KS et al. Small 2016;12:2173–85.