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Cubic Liquid Crystalline Nanoparticles for Co-Delivery of siRNA and Drugs in Alzheimer's Therapy

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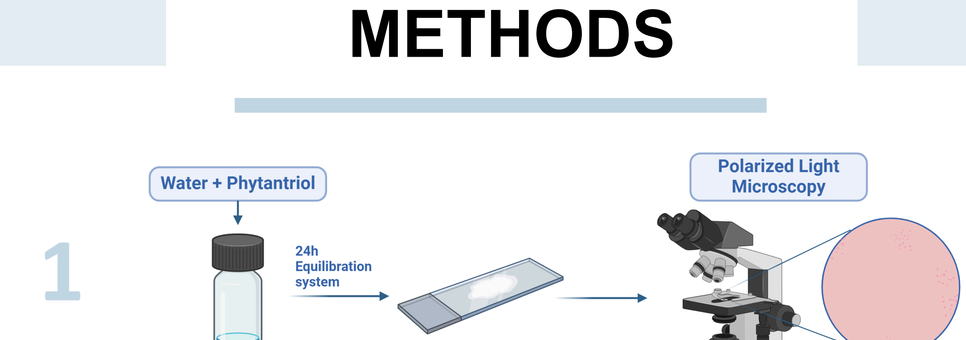
INTRODUCTION

Alzheimer's disease (AD) is a neurological disorder marked by cognitive decline and motor impairment, with origins that remain partially understood [1]. To address the limitations of conventional treatments, this study proposes a combined gene-silencing approach with an anti-inflammatory drug. Phytantriol-based cubic liquid crystalline nanoparticles were developed to co-deliver BACE-targeting siRNA and piperine via intravenous administration, focusing on optimizing drug loading and surface properties, including a positive charge and stealth effect.

METHODS



RESULTS

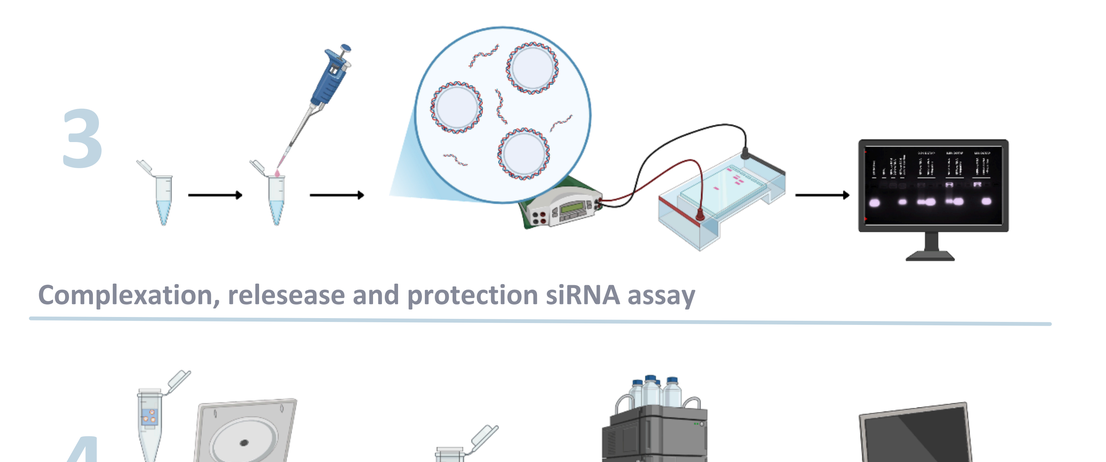


Fig 1 . Binary phase diagram of phytantriol in presence of diferent amounts of water

References:[1] Scheltens et al, Lancet, 2021. doi:10.1016/S0140-6736(20)32205-4.

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RESULTS

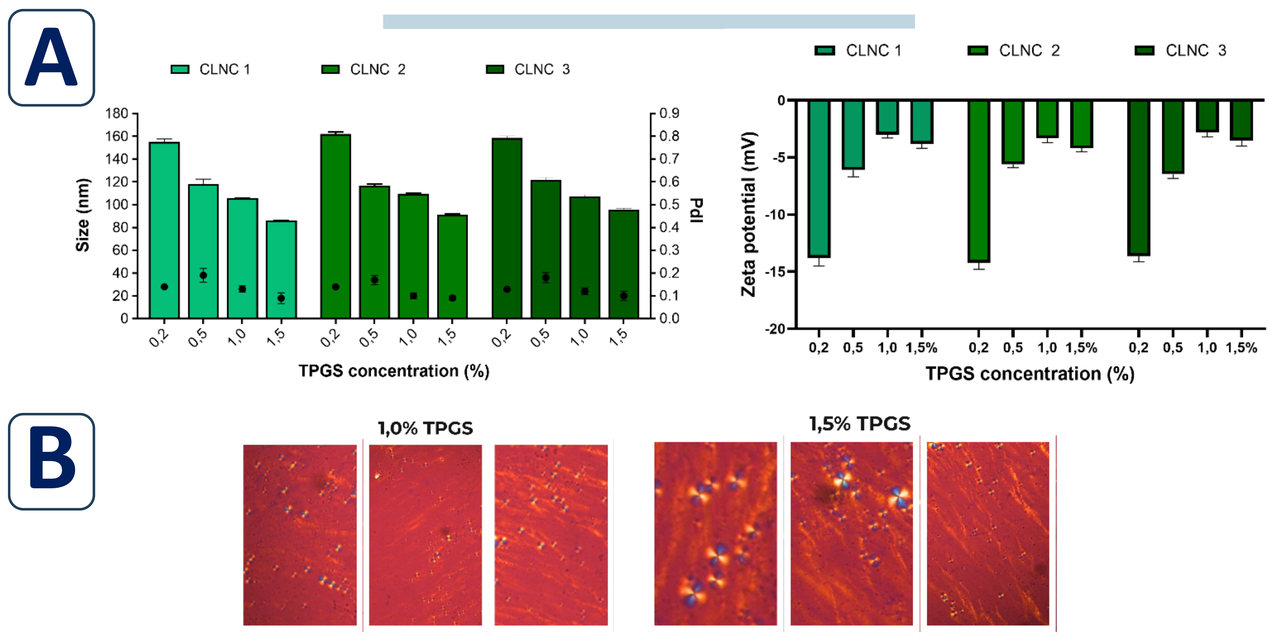

Fig 2. (A) Colloidal Properties of phytantriol-based CLCNs with Vit E. TPGS **(B)** Influency of TPGS on phytantriol bulk gel analysed by polarizing microscopy.

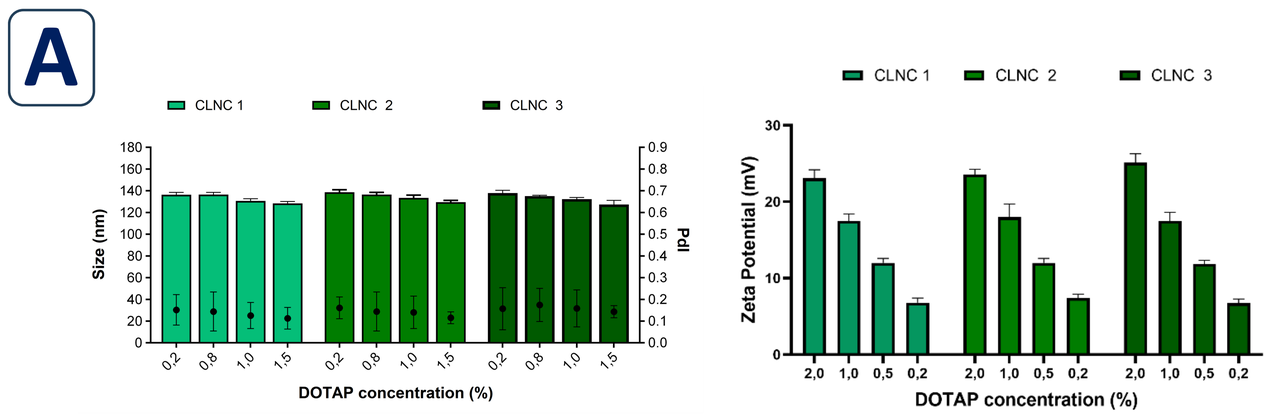

Fig 3. (A) Colloidal properties of phytantriol-based CLCNs with Vit E. TPGS+DOTAP **(B)** Influency of DOTAP on mesofase behaviour of phytantriol+TPGS bulk gel

Table 1 . Colloidal properties of phytantriol-based CLCNs with Vit E. TPGS+PAH

CLNC	Size (nm)	PdI	Zeta Potential (mV)
CLCN+ 0.5% PAH	155.7±0.777	0.168±0.021	0.269±0.510

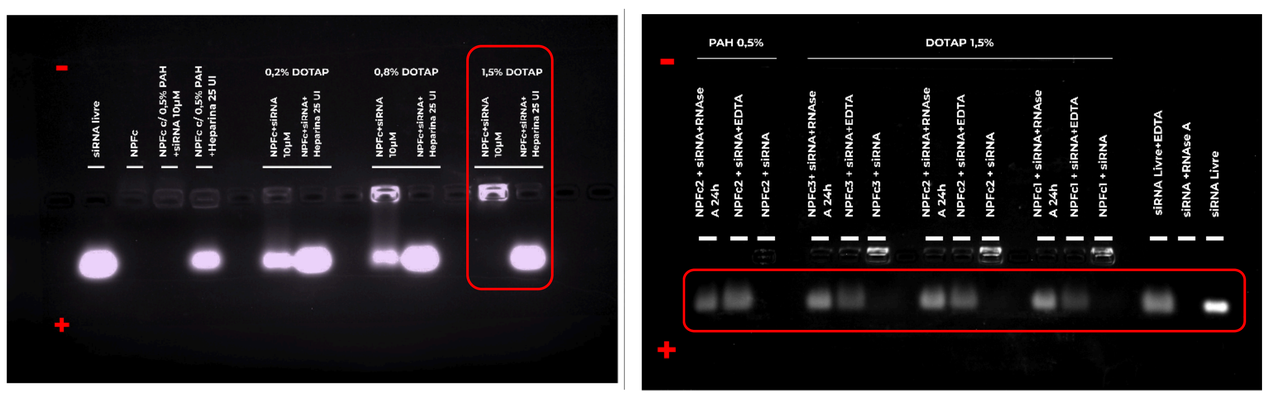

Fig 4 . (A) Electrophoretic profile of siRNA complexation and release by CLCNs at different DOTAP concentrations **(B)** Electrophoretic profile of CLCNs-mediated protection of siRNA against RNase A

Table 2 . Colloidal properties of phytantriol-based CLCNs and their piperine (PIP) encapsulation efficiency

CLNCs	Size (nm)	PdI	Zeta Potential (mV)	EE(%)
CLCN 1 + 0.05%PIP	136.2±1.67	0.129±0.01	+23.3±1.83	94.63±1.5
CLCN 2 + 0.05%PIP	138.9±3.90	0.109±0.03	+19.5±0.80	95.56±0.47
CLNC 3 + 0.1%PIP	131.4±1.10	0.081±0.02	+20.8±0.85	97.75±0.20
CLNC 4 + 0.05%PIP	155.7±0.77	0.168±0.02	+0.26±0.51	96.48±0.30

CONCLUSION

Phytantriol formed stable cubic liquid-crystalline structures, with Vitamin E TPGS below 1% enhancing CLCNs stability without phase transitions. The CLCNs successfully encapsulated piperine and the presence of DOTAP or PAH complexed and protected siRNA from RNase. The results showed a promise potential of CLCNs to co-deliver siRNA and drug in the treatment of AD.