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Self-assembly of Azacitidine Prodrugs for the Treatment of Myelodysplastic Syndromes Amphiphilic prodrug

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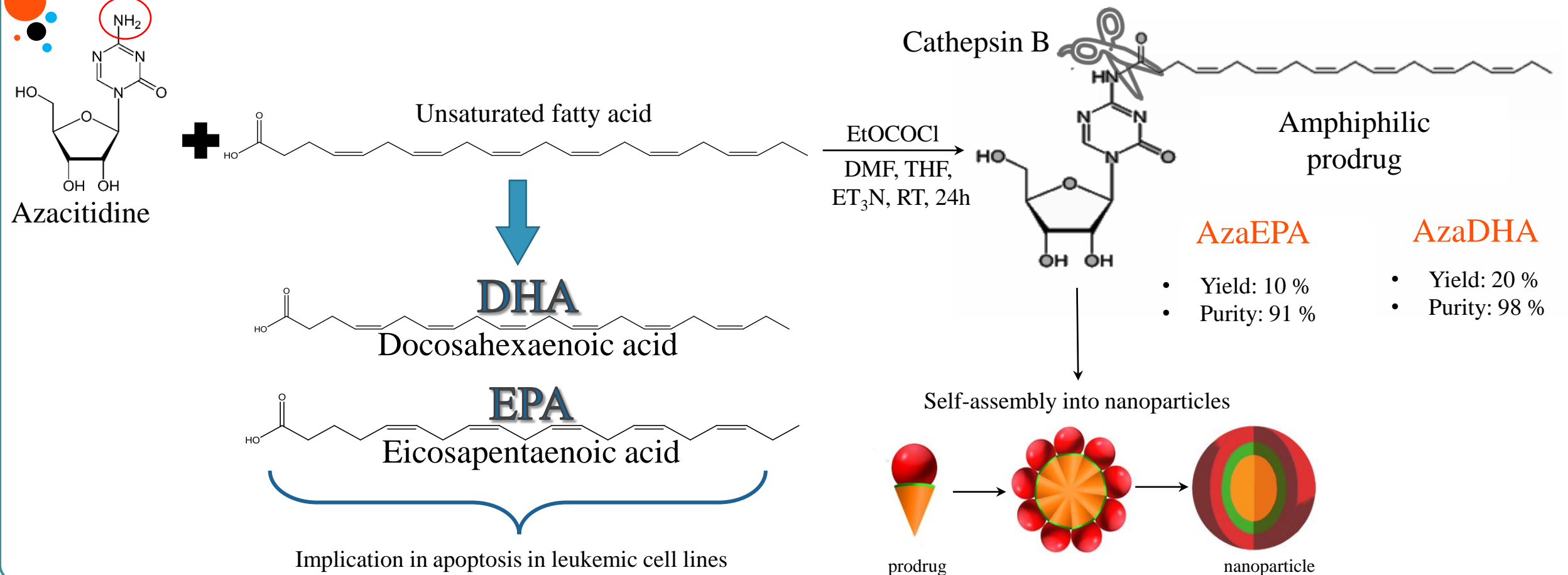
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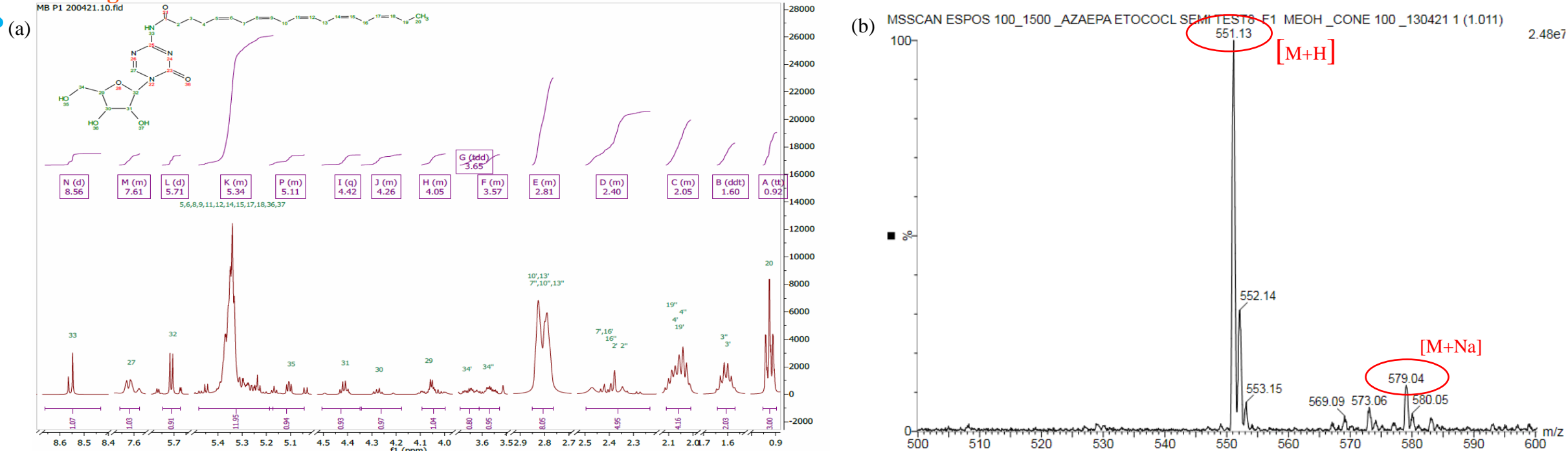
Introduction

5-azacytidine is a hypomethylating agent used for the treatment of myelodysplastic syndromes. However, after administration, it exhibits several limitations including restricted diffusion and cellular internalization due to its hydrophilicity and rapid enzymatic degradation. **Our objective is to improve the drug diffusion and to protect it from metabolic degradation via the synthesis of an amphiphilic prodrug and its formulation into self-assemblies.**

1. Prodrug synthesis

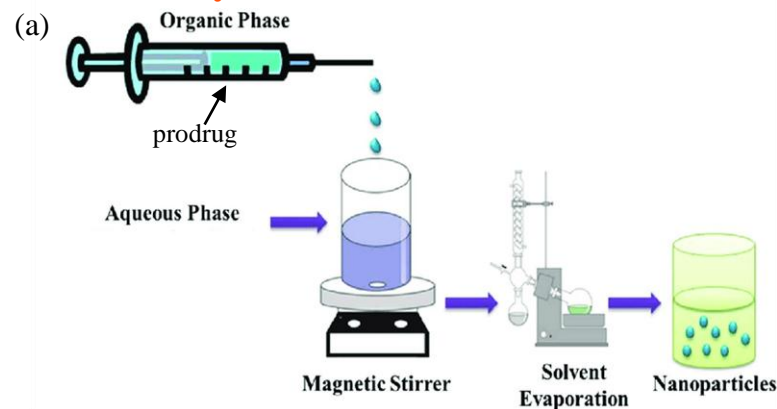


2. Prodrug characterization



(a) ¹H NMR spectroscopy of the AzaEPA prodrug, (b) Mass spectrometry of the AzaEPA prodrug. Similarly the AzaDHA prodrug was identified using the same methods.

3. Self-assembly formulation and characterization



(b) AzaEPA

Z Average diameter	Zeta potential	PDI
183.3 nm ± 0.7 %	-2.4 mV ± 29.5 %	0.11 ± 10.2 %

AzaDHA

Z Average diameter	Zeta potential	PDI
164.2 nm ± 0.5 %	-3.2 mV ± 12.3 %	0.10 ± 5.6 %

(a) Nanoprecipitation process used to obtain self-assemblies

(b) Dynamic Light Scattering (DLS) measurements of the obtained self-assemblies

Conclusion

An azacitidine prodrug was achieved via conjugating azacitidine to a fatty acid. The obtained prodrug self-assembles through nanoprecipitation to produce nanoparticles, that have been characterized. Finally, *in vitro* studies will be performed to determine the biological efficacy of these nanoparticles.