IOCN 2023
The 4th International Online Conference on Nanomaterials
05–19 May 2023 | online

4-Ammoniumbutylstyrene Based-Nanoparticles for the Controlled Release of Fenretinide

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DIPARTIMENTO DI FARMACIA
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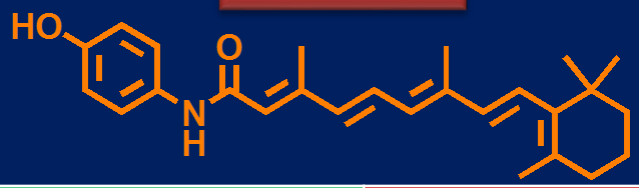
DIFAR

Graphical Abstract

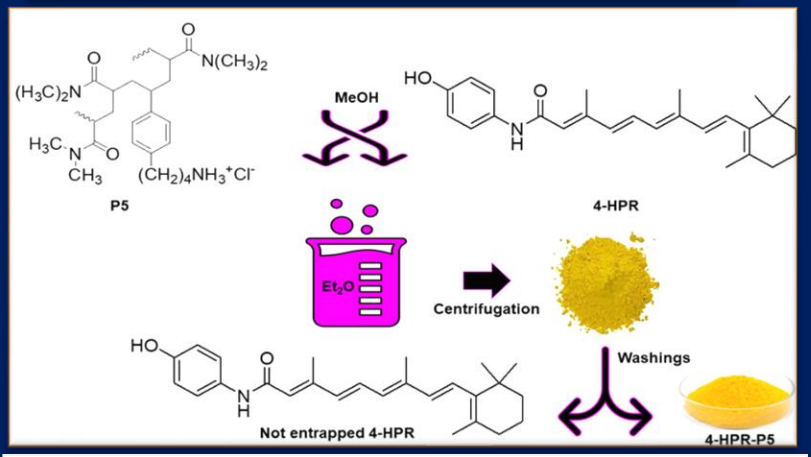
FENRETINIDE

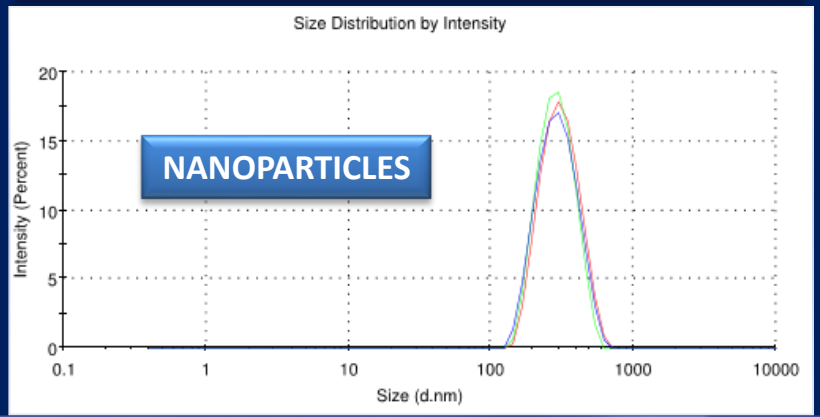


PROS	CONS
HIGH ANTITUMOR ACTIVITY	LOW SOLUBILITY
FAVORABLE TOXICOLOGIAL PROFILE	POOR BIOAVALABILITY
NO INDUCTION OF RESISTANCE	CLINICAL TRIALS WITH HIGH VARIABILITY IN RESULTS

NEUROBLASTOMA CELLS

AMORPHOUS SOLID DISPERSION BY ANTI SOLVENT PRECIPITATION TECHNIQUE





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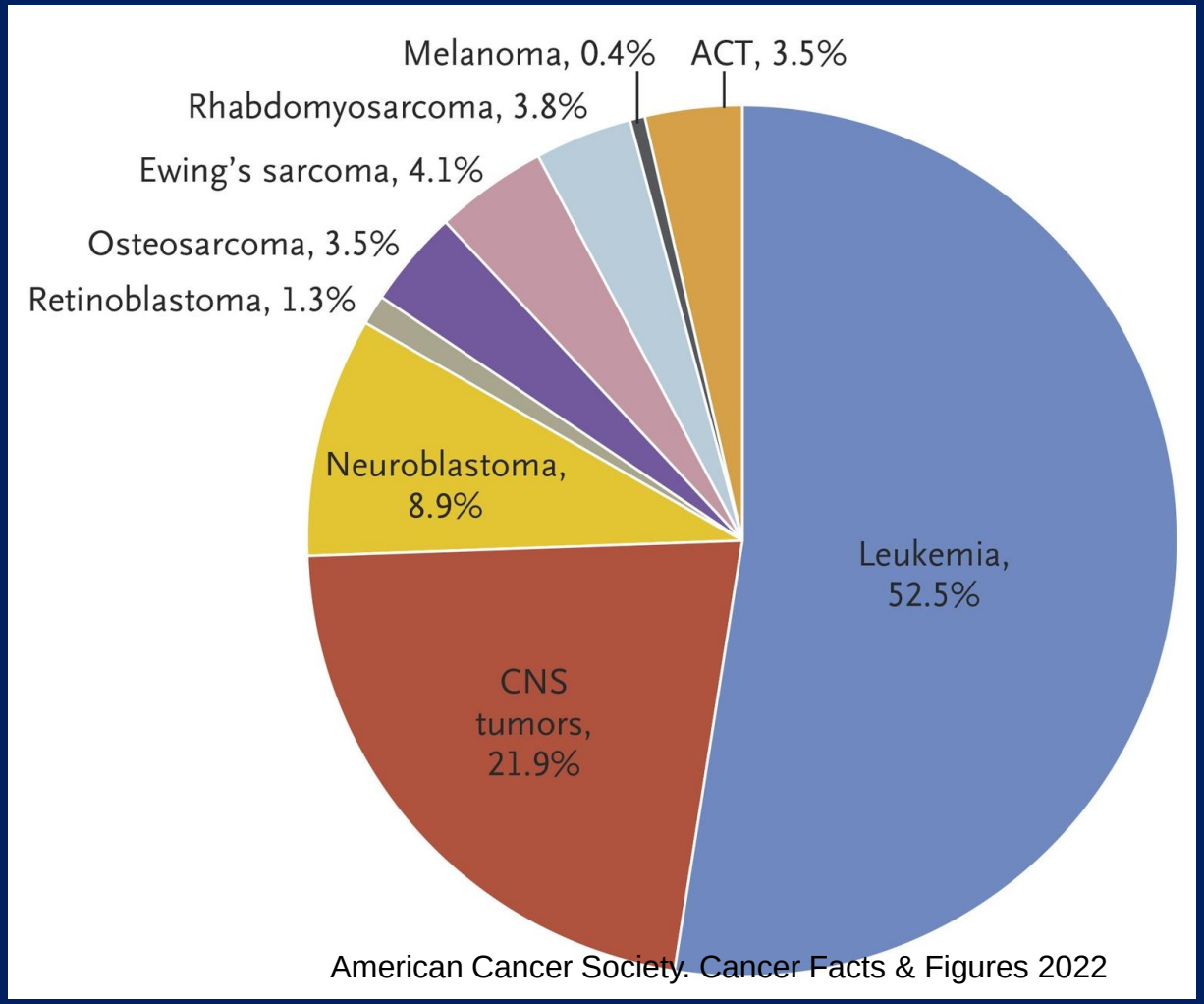
Abstract

Fenretinide (4-HPR), a synthetic retinoid with low toxicological profile, is endowed with high an-titumor activity. However, 4-HPR shows poor oral absorption due to its low solubility, and variable blood concentrations for a massive hepatic first pass effect. Here, we prepared nanoparticles (NPs) made of 4-ammoniunbutylstyrene random copolymer (P5) by the anti-solvent co-precipitation technique. The encapsulation led to an increase in drug apparent solubility of 1134 folds with a drug loading of 37%. The NPs showed an extended dissolution rate, a mean diameter of 249 nm, positive Zeta potential, and confirmed an anti-proliferative activity on neuroblastoma cells.

Keywords: Fenretinide; Drug Delivery; Nanoparticles, Neuroblastoma

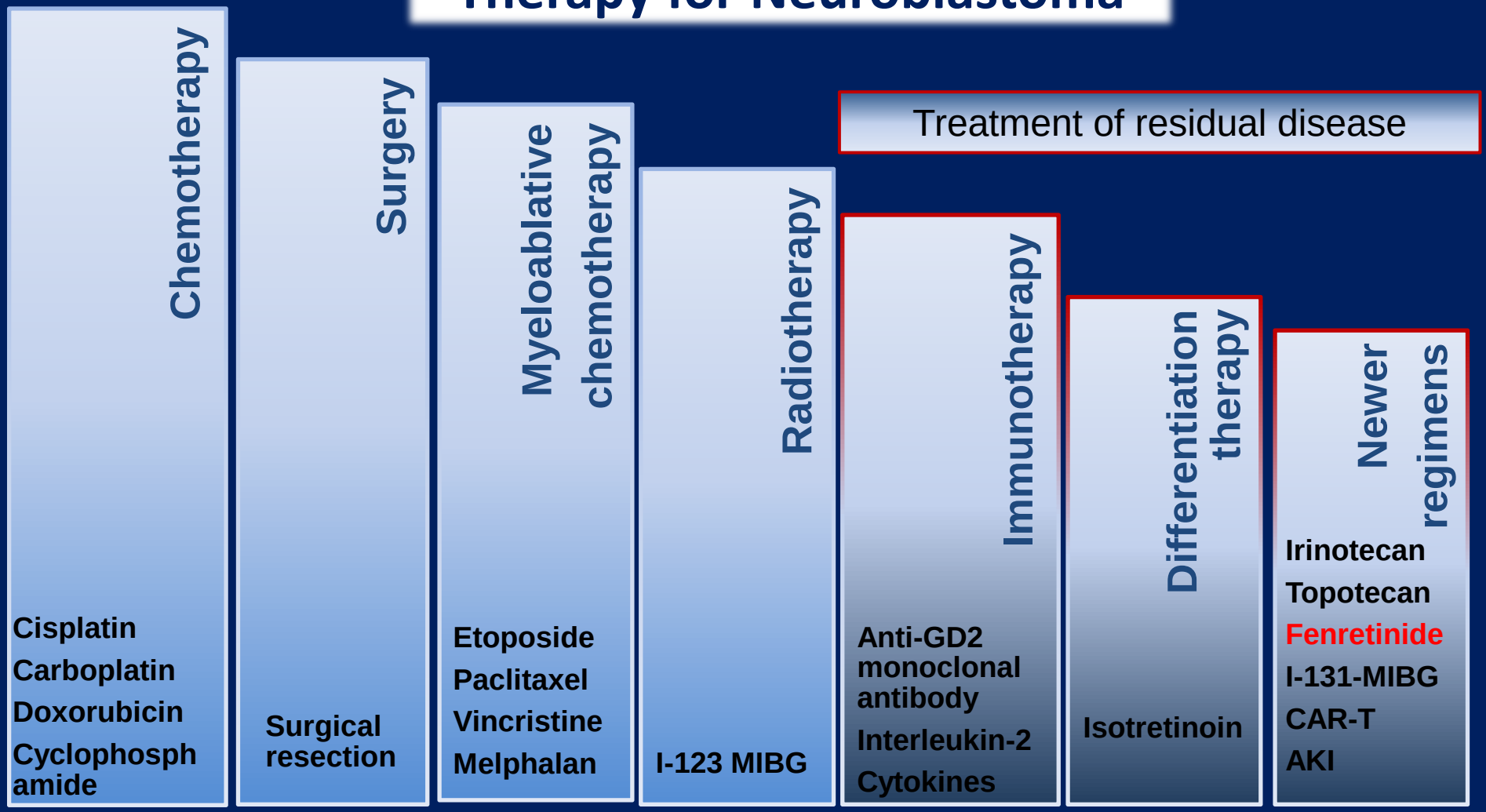
Frequency of Paediatric Cancer Types

1 in 7,000 children

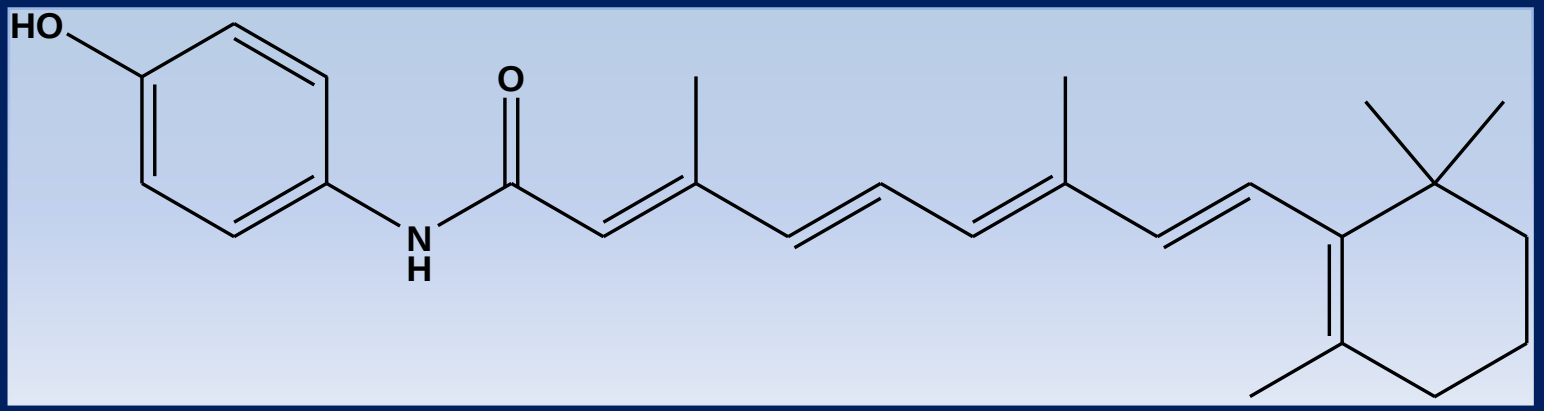


American Cancer Society. Cancer Facts & Figures 2022

Therapy for Neuroblastoma



Fenretinide



N-(4-hydroxyphenyl)retinamide (4-HPR)

PROS	CONS
HIGH ANTITUMOR ACTIVITY	LOW SOLUBILITY
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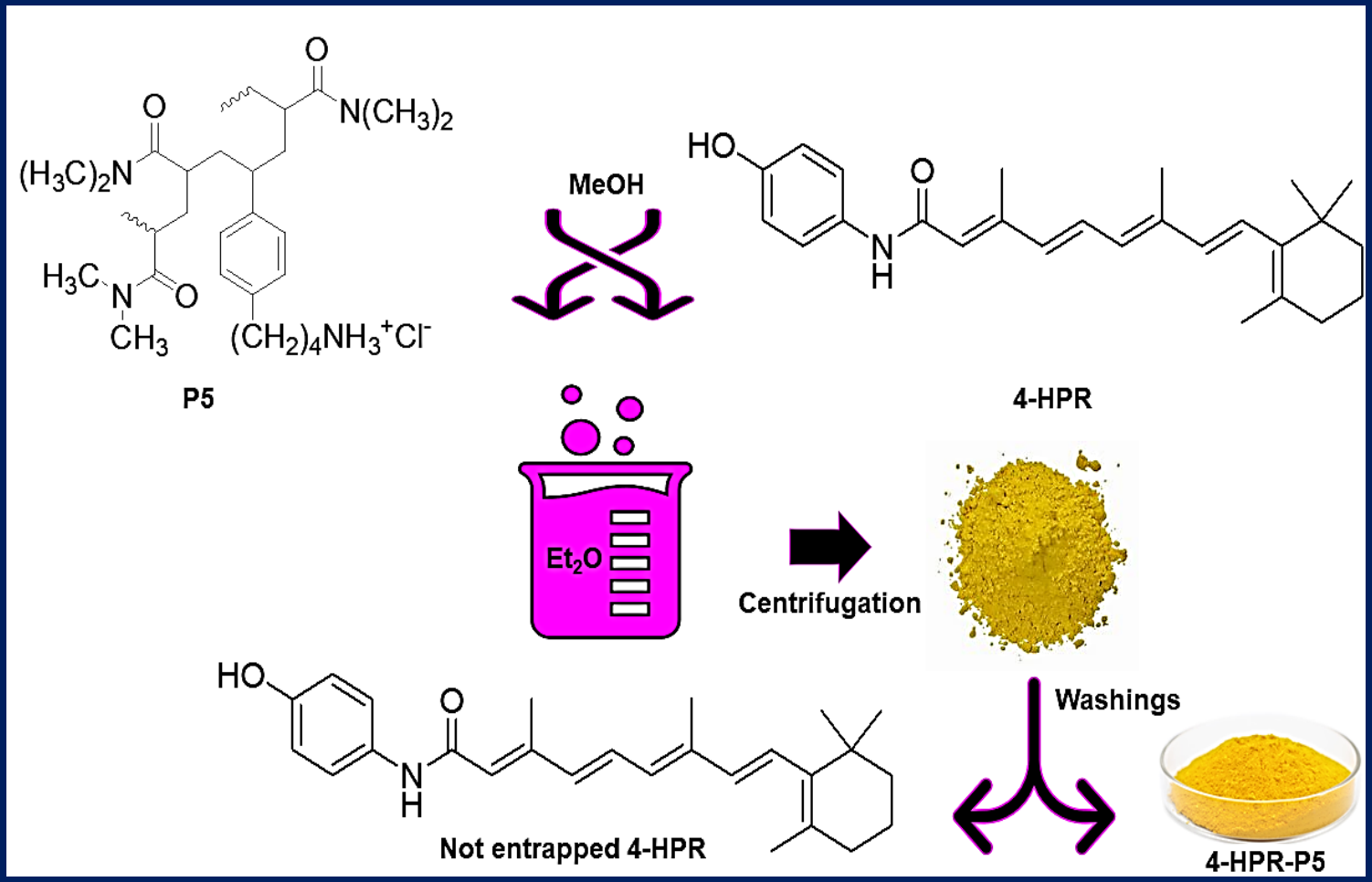
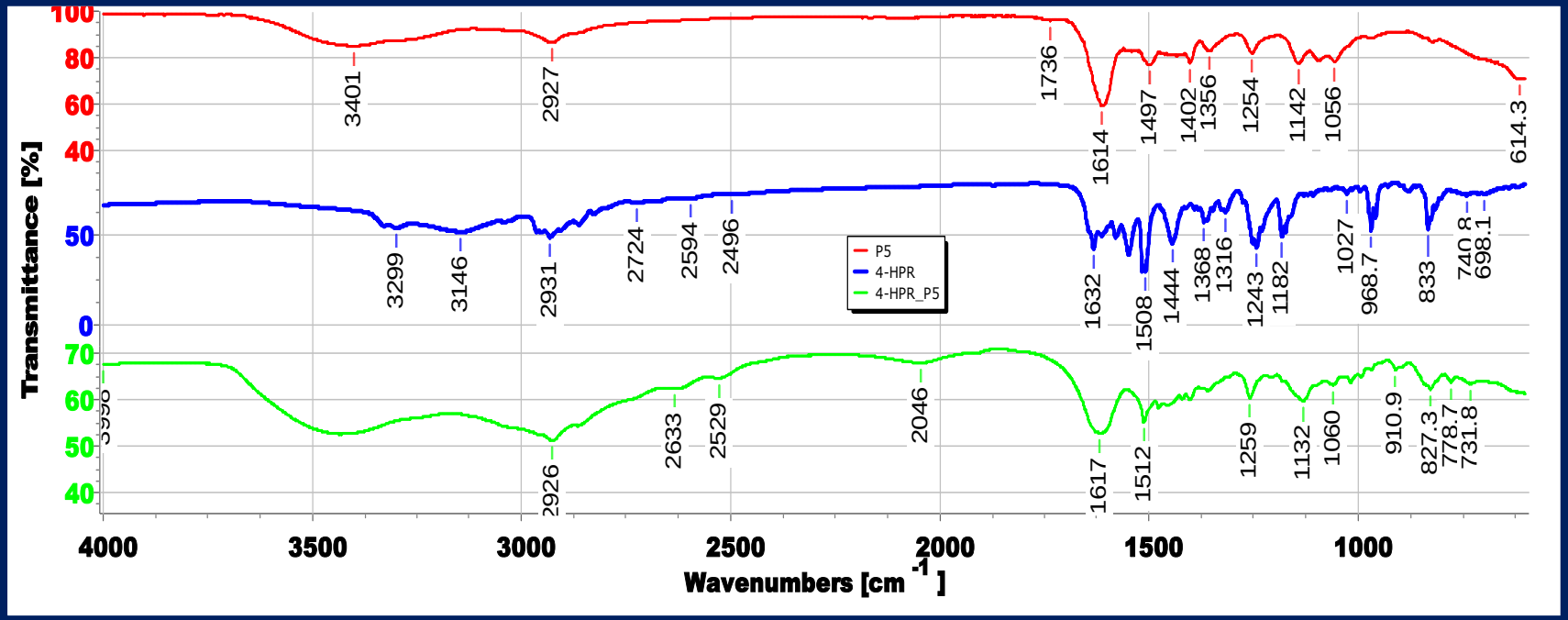
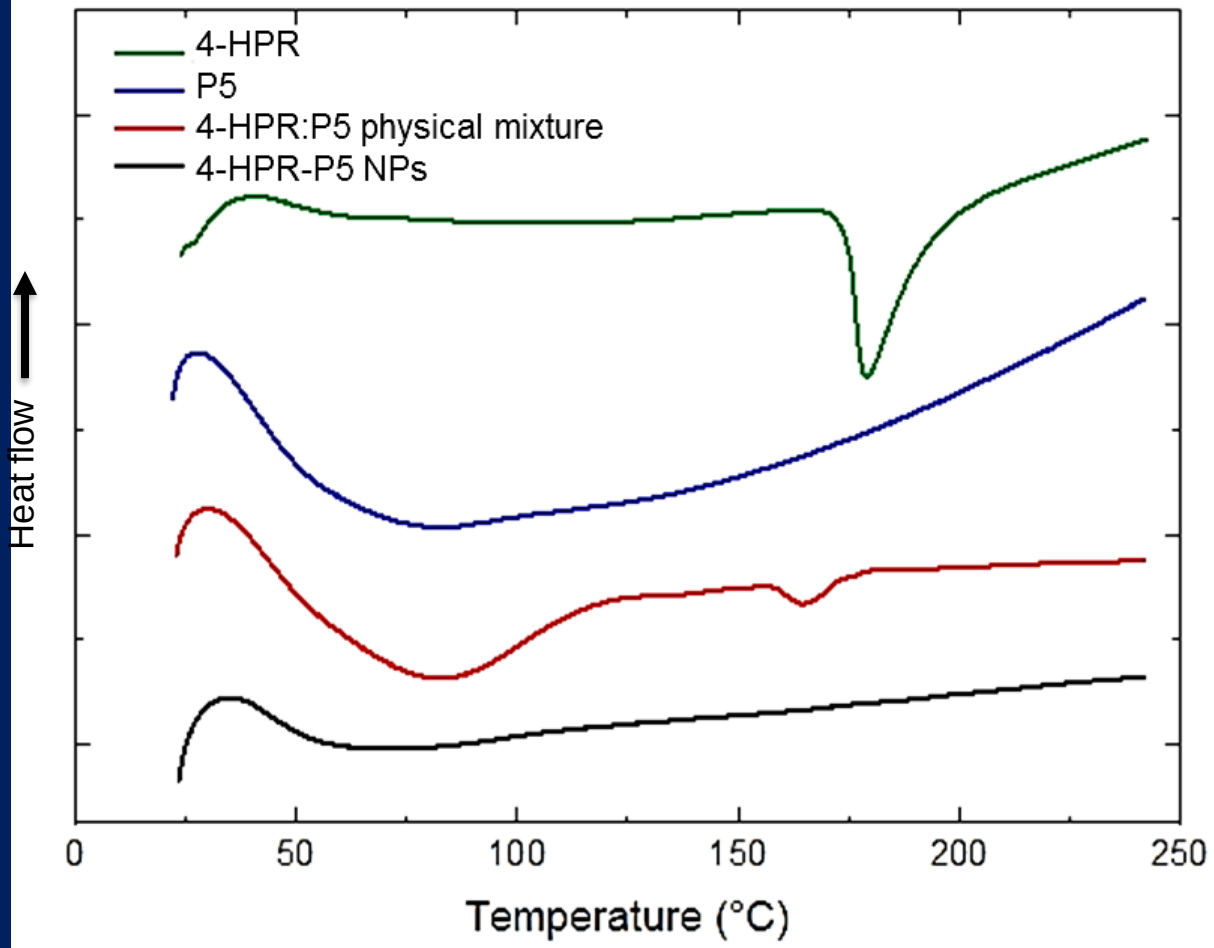
Preparation of 4-HPR-P5 NPs



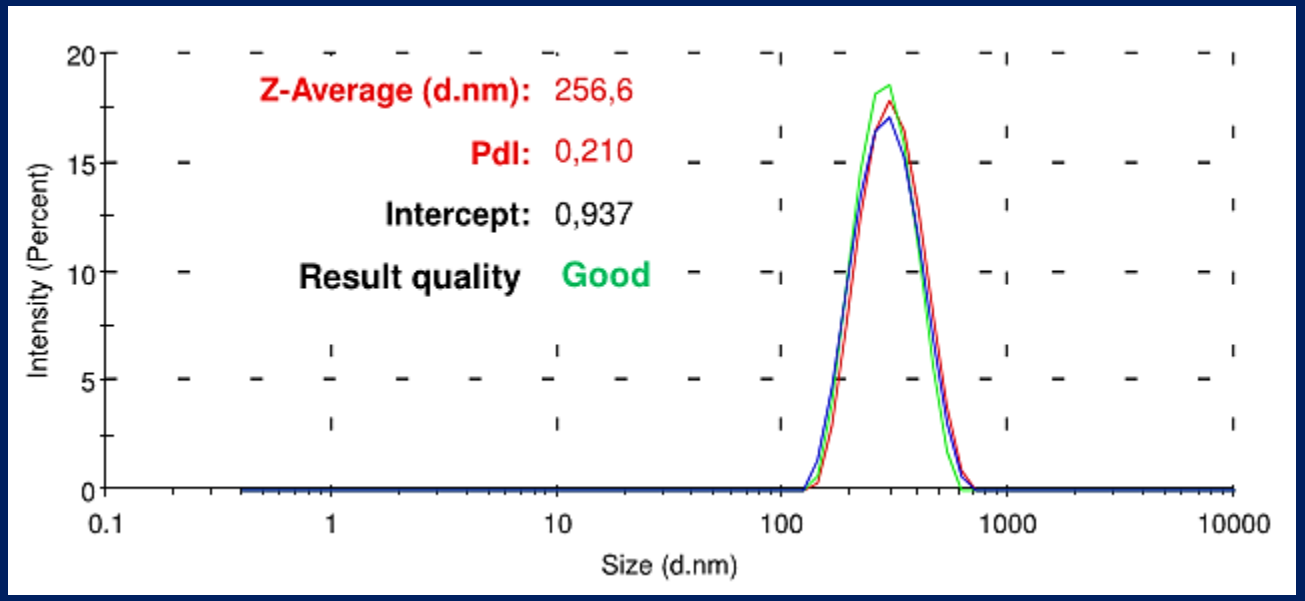
FTIR spectra of 4-HPR-P5 NPs P5 and pristine 4-HPR

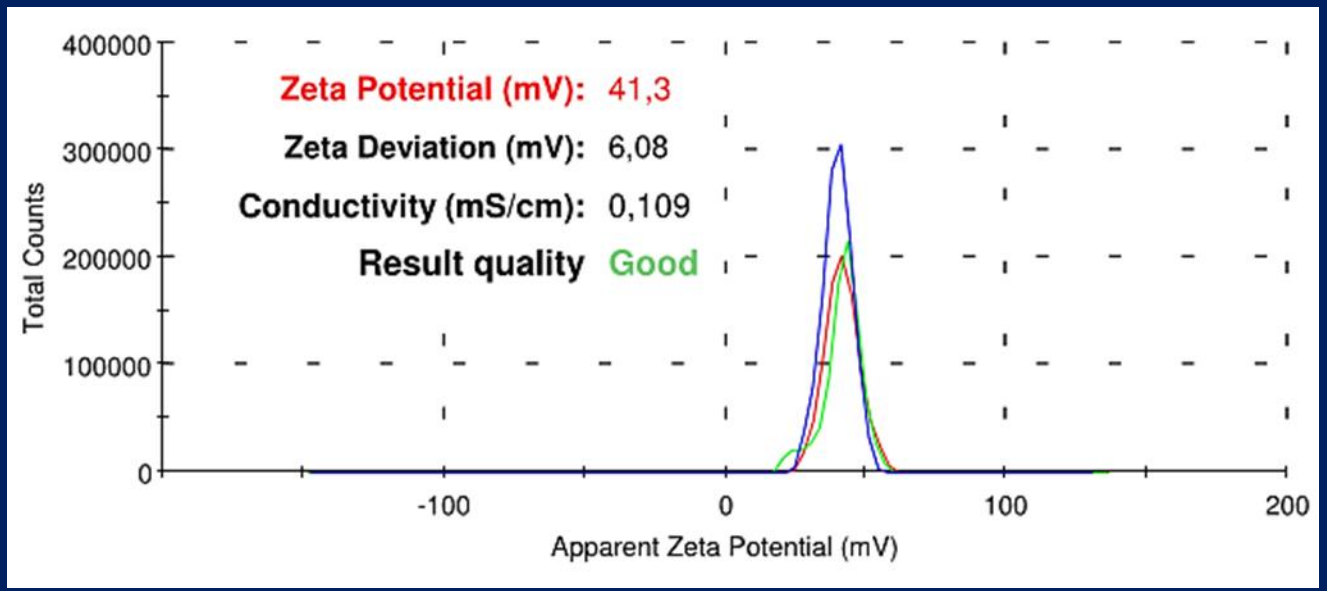


DSC thermograms

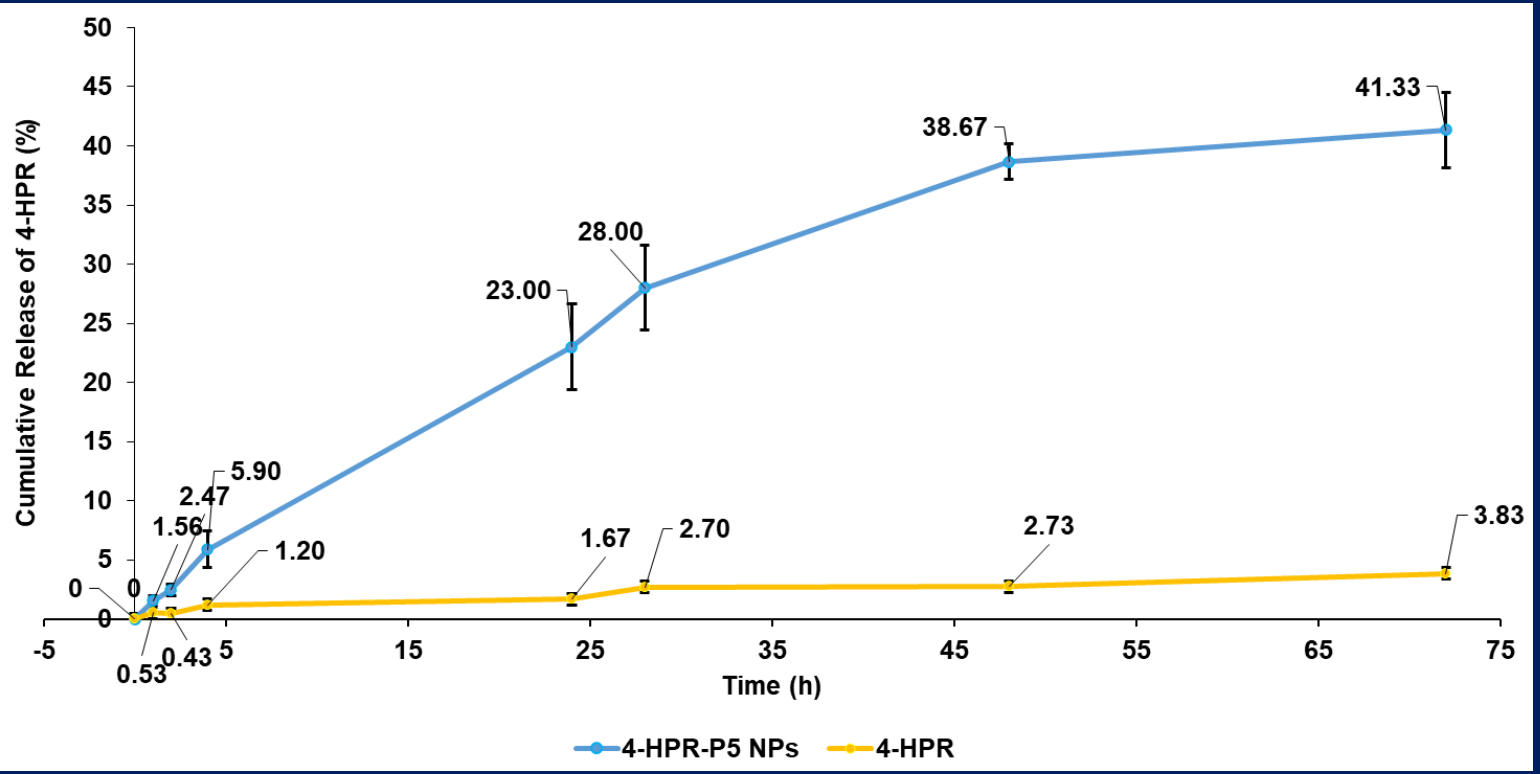


DLS analysis





In vitro drug release



IC50 VALUES

Cells	Times (h)	4-HPR (μM)	P5 (μM)	4-HPR-P5 NPs (μM)
IMR-32	24	1.08	-	1.07
	48	1.93	-	1.76
	72	0.68	-	1.25
SH-SY5Y	24	7.84	-	-
	48	4.32	-	-
	72	4.99	-	1.93

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