





## Lipidic Cubic-Phase Nanoparticles (Cubosomes) Loaded with Doxorubicin and Labeled with <sup>177</sup>Lu as a Potential Tool for Combined Chemo and Internal Radiotherapy for Cancers

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Figure S1. <sup>1</sup>H NMR spectrum of *p*-NCS-benzyl-DOTAGA-oleylamine in DMSO-*d6* (298 K).



Figure S2. <sup>13</sup>C NMR spectrum of *p*-NCS-benzyl-DOTAGA-oleylamine in DMSO-*d6* (298 K).



Figure S3. ESI-MS spectrum of *p*-NCS-benzyl-DOTAGA-oleylamine.

Time (h)	PDI	Zeta Potential (mV)
0	$0.16\pm0.03$	$-28.7\pm0.4$
8	$0.19\pm0.01$	$-25.9 \pm 1.3$
24	$0.19\pm0.01$	$-23.5 \pm 1.2$
48	$0.16\pm0.02$	$-22.9 \pm 1.1$
72	$0.21\pm0.01$	$-23.3 \pm 1.3$
96	$0.23 \pm 0.01$	$-21.9 \pm 0.8$

Table S1. Stability of the blank cubosomes in time.

DOX Cubosomes		
<b>Incubation Time</b>	<i>IC</i> 50 (μg/mL)	
24 h	$1.26 \pm 0.33$	
48 h	$0.51\pm0.14$	
72 h	$0.20\pm0.09$	
7211	$0.20 \pm 0.09$	



**Figure S4.** Viability of HeLa cells treated with cubosomes at various GMO concentrations. Non-treated cells were used as a control. Data points and SD are taken from three or more measurements. Statistical significance was considered if  $p \le 0.05$  (\*).



**Figure S5.** UV-Vis spectra of DOX solution in 25 °C (blue line) and heated to 95 °C (measured at 25 °C following equilibration after heating – pink line).



**Figure S6.** Viability of HeLa cells treated with acetate buffer, acetate buffer with DOX and acetate buffer with DOX heated in 95 °C. Non-treated cells were used as a control. Data points and SD are taken from three or more measurements. Statistical significance was considered if  $p \le 0.05$  (\*),  $p \le 0.01$  (\*\*) and  $p \le 0.001$  (\*\*\*).



**Figure S7.** Viability of HeLa cells treated with cubosomes doped with: DOTAGA-OA-<sup>177</sup>Lu (<sup>177</sup>Lu) and DOX DOTAGA-OA-<sup>177</sup>Lu (<sup>177</sup>Lu + DOX). Data points and SD are taken from three or more measurements. Statistical significance was considered if  $p \le 0.05$  (\*),  $p \le 0.01$  (\*\*),  $p \le 0.001$  (\*\*\*) and  $p \le 0.0001$  (\*\*\*).



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