Sugar-Decorated Cholesterol-Core Nanoparticles as Potential Targeting Nanomedicines for the Delivery of Lipophilic Drugs

Laís Rossetto Ferraz de Barros,[†] Carlos Eduardo de Castro,[†] Anabella Patricia Rosso,[†] Rodrigo da Costa Duarte,[‡] Alexandre Gonçalves Dal-Bó,[‡] Wendel Andrade Alves,[†] and Fernando Carlos Giacomelli,[†]*

[†] Centro de Ciências Naturais e Humanas, Universidade Federal do ABC, 09210-580, Santo André, Brazil

[‡] Universidade do Extremo Sul Catarinense - UNESC, 88806-000, Criciúma, SC, Brazil

* Corresponding Author: Fernando Carlos Giacomelli

e-mail: fernando.giacomelli@ufabc.edu.br

Spectroscopic Characterization

The spectroscopic characterization was performed by Nuclear Magnetic Resonance (Bruker Avance III) in $CDCl_3$ and DMSO for ^{13}C NMR spectroscopies, at 400 and 100 MHz, respectively. The chemical shifts (δ) are reported in parts per million (ppm), relative to tetramethylsilane TMS (0.00 ppm), and the coupling constants (J) are reported in Hz. Low-resolution mass spectra were recorded on a Bruker DaltonicsAutoflex apparatus for MALDI FTIR spectra were acquired with a Shimadzu IR Prestige-21, with a resolution of 4 cm^{-1} using KBr pellets (600 – 4000 cm^{-1}).

Chol-PEO_{22}-N_3 (2): N,N'-dicyclohexylcarbodiimide (DCC) (0.680g, 3.3 mmol) and 4-dimethylaminopyridine (DMAP) (0.092g, 0.75mmol) were added into a stirred solution of PEO_{22}-N_3 (3.27 g, 3.1 mmol) and hemisuccinate cholesteryl **(1)** (1.51g, 3.1 mmol) in anhydrous methylene chloride (40 mL). The reaction was monitored by TLC, and after 48h at room temperature under N_2 atmosphere, the mixture was filtered over a pad of Celite® and evaporated under reduced pressure to give an oily, colorless product. Pure glycosurfactant azide-poly(ethylene glycol)-cholesterol conjugate Chol-PEO_{22}-N_3 (2) (3.4g, 72%) was isolated after purification by silica gel flash column chromatography using methylene chloride:methanol (15:1 *v*/*v*) as eluant. FTIR (solid state, KBr νmax/cm^{-1}): 2934, 2870, 2105 (azide absorbance peak 2100 cm^{-1}), 1733, 1643, 1468, 1455, 1351, 1300 1251, 1107, 1034, 951, 846. ^{13}C NMR (100MHz, $CDCl_3$): δ 172.74, 172.01, 139.94, 123.04, 74.73, 71.03, 70.36, 69.42, 64.14, 57.04, 56.50, 51.05, 50.37, 42.67, 39.87, 38.41, 37.31, 36.94, 36.54, 36.14, 34.29, 32.25, 29.79, 29.52, 29.48, 28.57, 28.36, 28.08, 25.97, 25.29, 24.63, 24.18, 23.16, 22.91, 19.66, 19.07, 12.21. MALDI-TOF MS calcd for $C_{77}H_{141}N_3O_{26}$: m/z 1523.98, found: m/z 1547.83 $[M + Na]^+$.

Chol-PEO$_{22}$-GlcNAc (3): Copper sulfate (0.081g, 0.51mmol) and sodium ascorbate (0.101g, 0.51mmol) were added into a stirred solution of propargyl-2-acetamido-2-deoxy-β-D-glucopyranoside (0.168g, 0.65 mmol) Chol-PEO$_{22}$-N$_3$ (2) (0.77 g, 0.51 mmol) in water/THF (1:1 v/v). The mixture was heated at 40°C and the reaction was monitored by TLC. After 24h, the solution was concentrated under vacuum. The residue was taken up in methylene chloride, filtered and concentrated. Pure Chol-PEO$_{22}$-GlcNAc **(3)** (0.64g; ≈ 70%) was isolated after silica gel flash column chromatography using methylene chloride: methanol (8:2 v/v) as eluent. FTIR (solid state, KBr νmax/cm^{-1}): 3406, 2932, 2906, 2871, 1798, 1731, 1654, 1468, 1465, 1351,1254, 1103, 1032, 952, 836, 750. ^{13}C NMR (100 MHz, DMSO) δ 173.22, 172.42, 171.71, 169.79, 163.50, 144.09, 139.90, 124.84, 122.55, 105.87, 100.67, 91.76, 88.33, 77.48, 75.28, 74.72, 73.89, 71.14, 68.69, 63.91, 61.74, 56.60, 55.77, 49.82, 42.31, 38.07, 36.53, 35.68, 31.83, 31.80, 29.04, 24.30, 23.45, 22.83, 21.02, 19.39, 12.10. MALDI-TOF MS calcd for $C_{88}H_{158}N_4O_{32}$: m/z 1783.26, found: m/z 1806.87 $[M + Na]^+$.

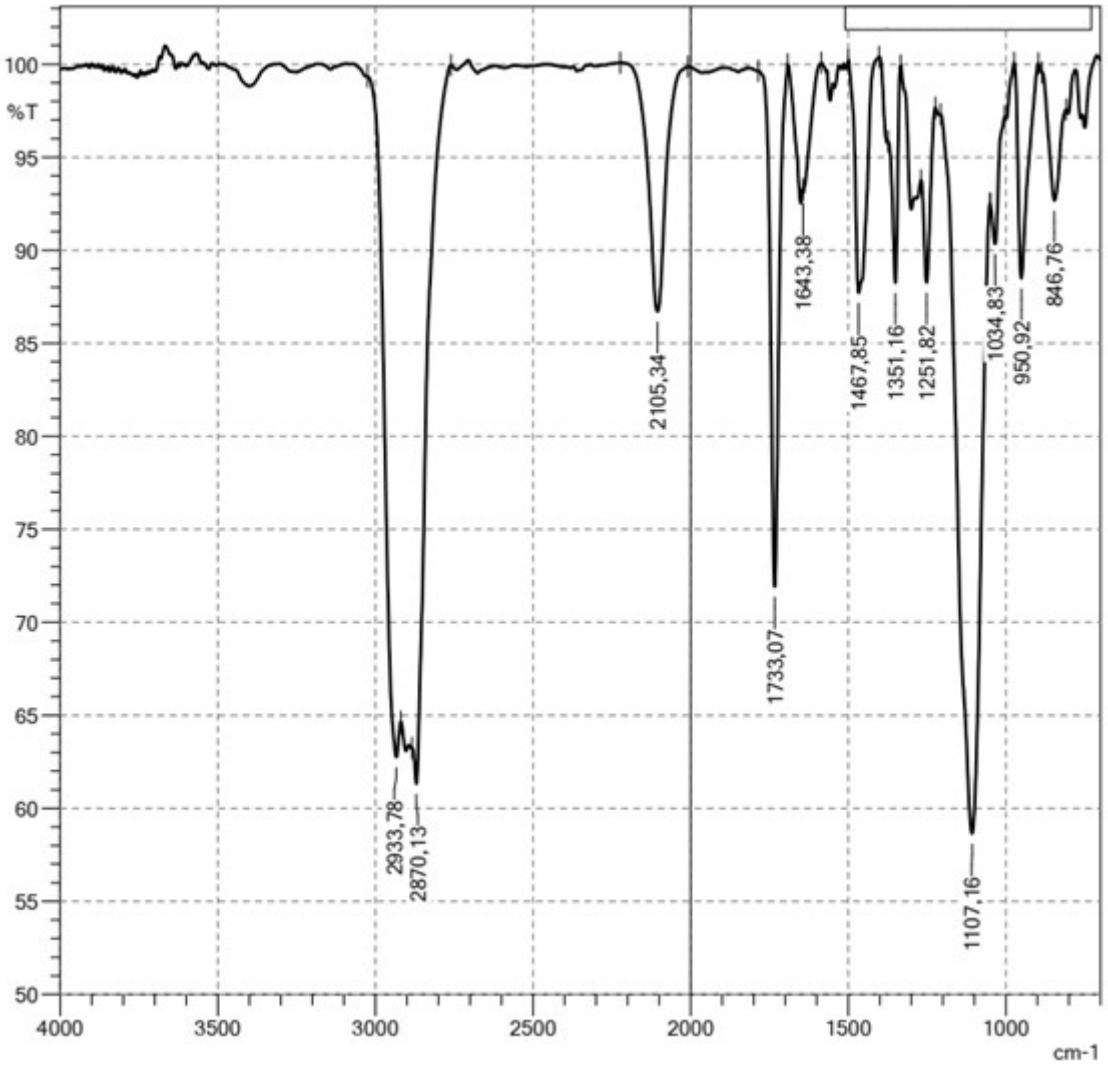

Figure S1. FTIR spectrum of Chol-PEO_{22}-N_3 **(2)**.

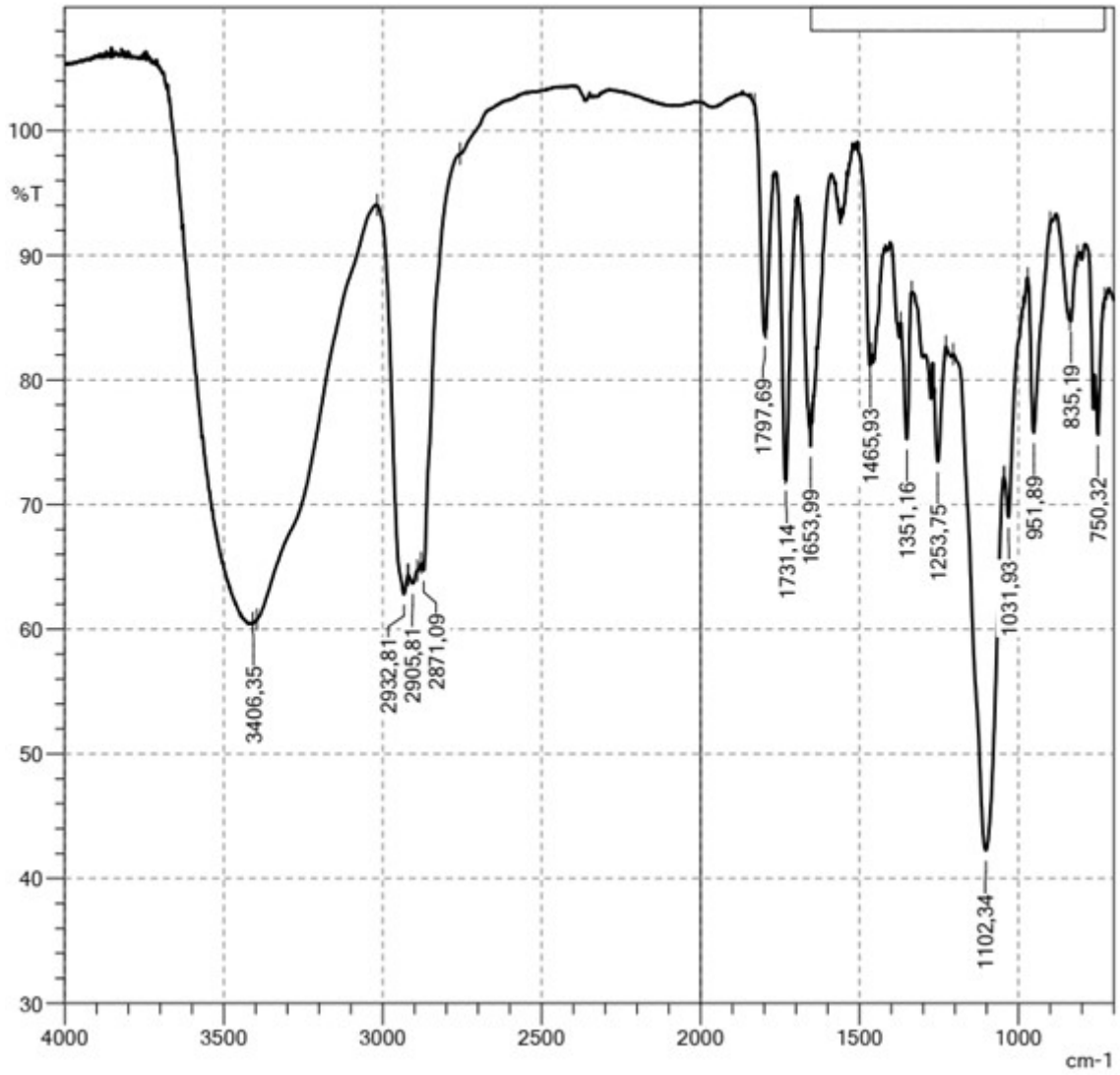

Figure S2. FTIR spectrum of Chol-PEO_{22}-GlcNAc **(3)**.

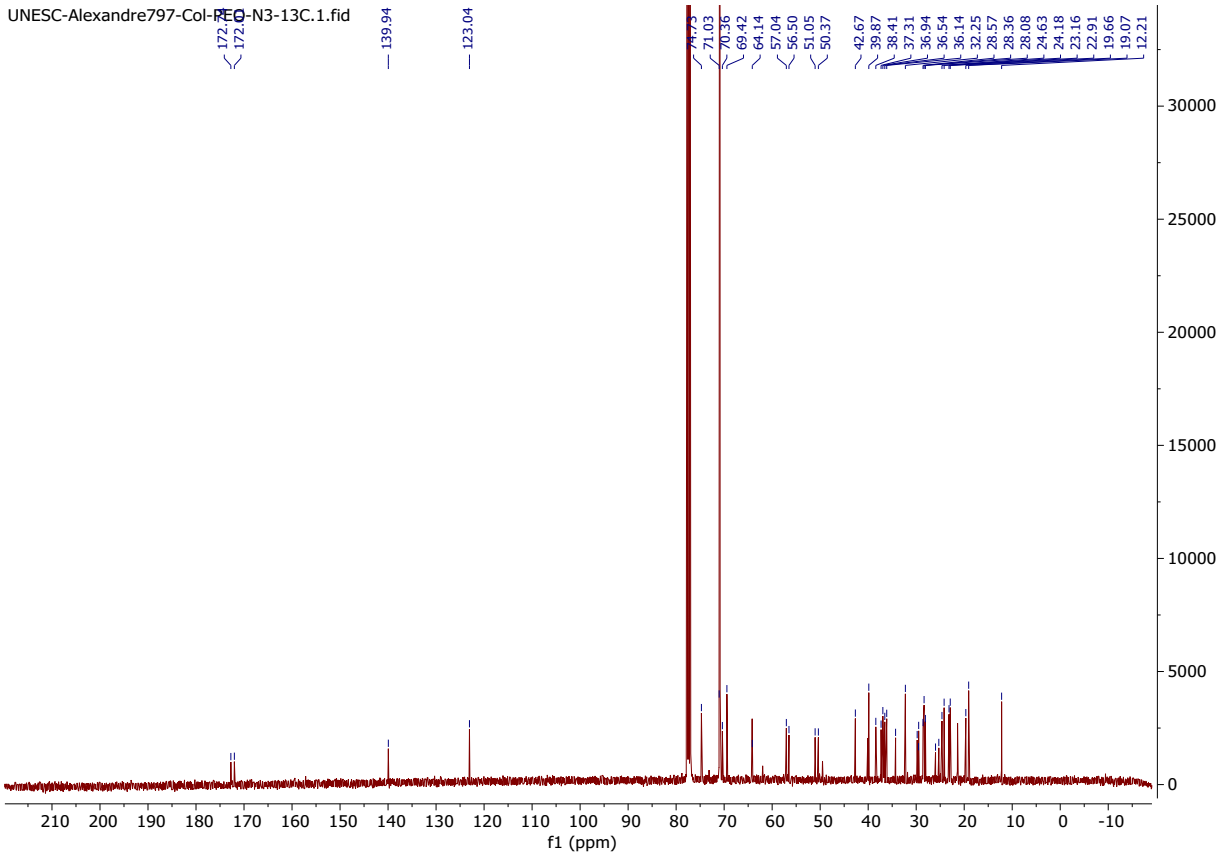

Figure S3. ^{13}C NMR spectrum of Chol-PEO_{22}-N_3 in $CDCl_3$.

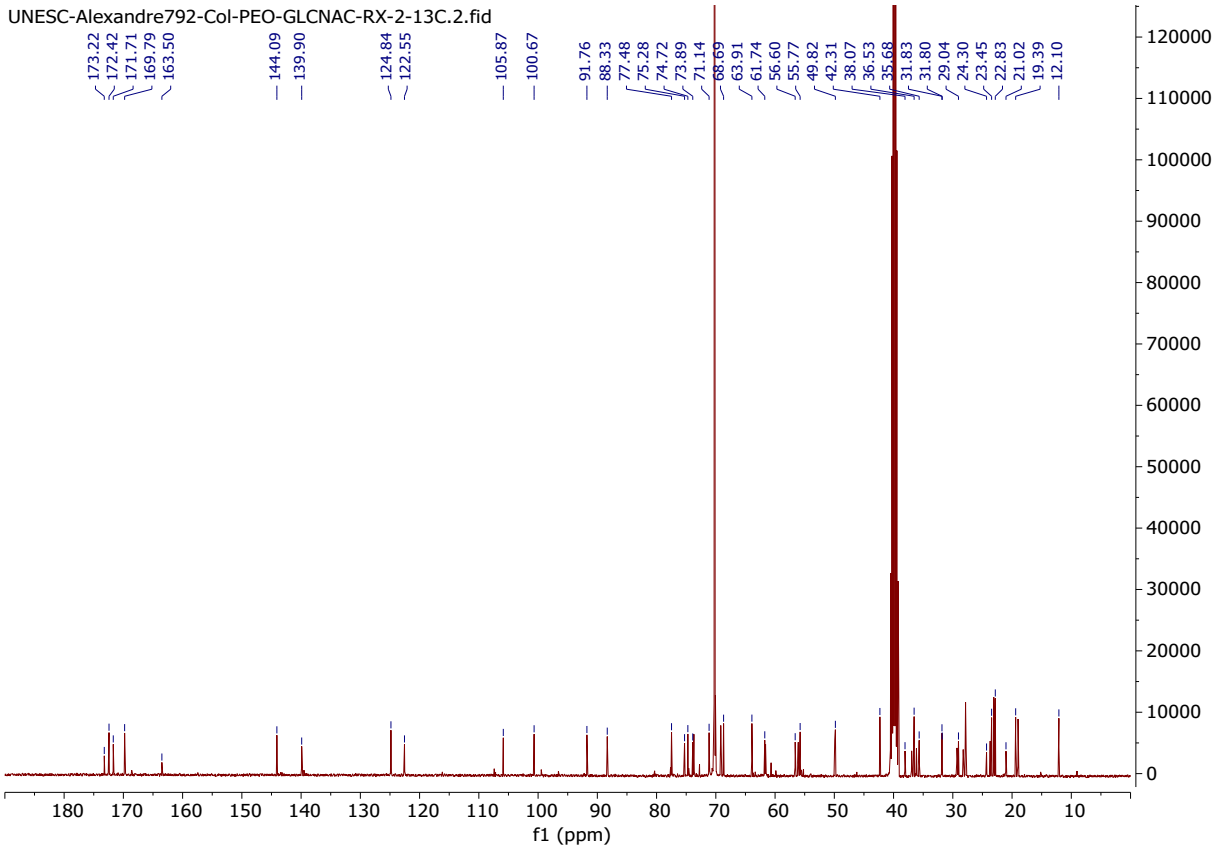

Figure S4. ^{13}C NMR spectrum of Chol-PEO_{22}-GlcNAc in DMSO.

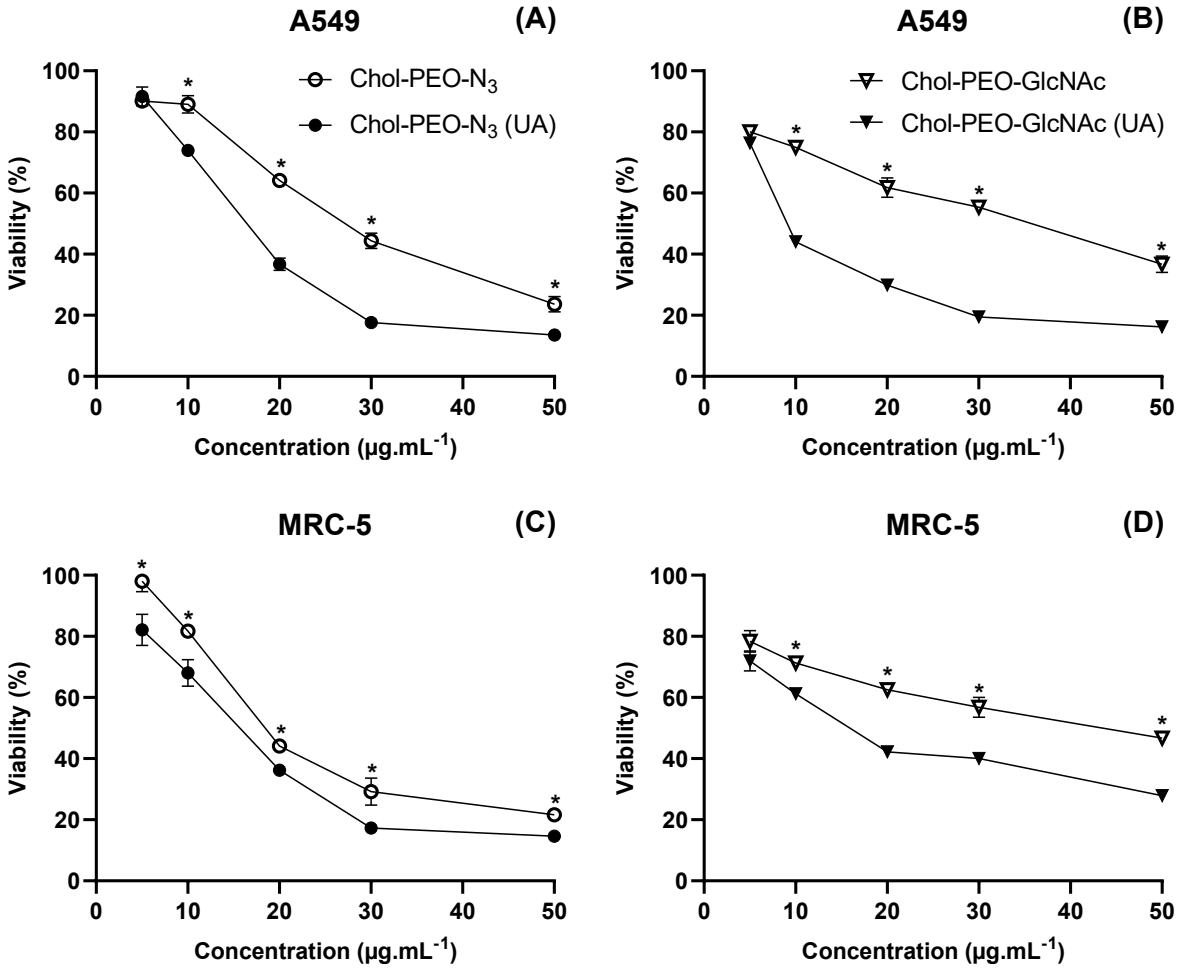

Figure S5. Viability of (A, B) A549 and (C, D) MRC-5 cells after 24 h exposure to various concentrations of UA-loaded and drug-free NPs (*$p < 0.05$ in comparison with groups treated with UA-loaded NPs as determined by two-way ANOVA with Bonferroni's multiple comparison test).