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Data Article

Data set on the synthesis and properties of 2',3'-dideoxyuridine triphosphate conjugated to SiO₂ nanoparticles



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ABSTRACT

SiO₂ nanoparticles were used as a transport system for cellular delivery of phosphorylated 2',3'-dideoxyuridine to increase its anticancer potency. This data set is related to the research article entitled "2',3'-Dideoxyuridine triphosphate conjugated to SiO₂ nanoparticles: synthesis and evaluation of antiproliferative activity" (Vasilyeva et al., 2018) [1]. It includes a protocol for the synthesis of 2',3'-dideoxyuridine-5'-{N-[4-(prop-2-yn-1-yloxy)butyl]-γ-amino}-triphosphate, its identification by NMR, IR and ESI-MS, experimental procedure of covalent attachment to SiO₂ nanoparticles with *via* Cu-catalyzed click-chemistry, experimental data on chemical stability of the conjugate at different pH values and cytotoxicity assessment of antiproliferative effect of the conjugate.

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Specifications table

Subject area	<i>Biochemistry, Chemistry, Nanobiotechnology</i>
More specific subject area	<i>Synthesis of phosphorylated nucleosides and their conjugation to SiO₂ nanoparticles</i>
Type of data	<i>Experimental synthesis protocols, Tables, Figures, Text file</i>
How data was acquired	<i>NMR, IR, mass spectrometry, analytical HPLC, MTT assay</i>
Data format	<i>Raw, Analyzed</i>
Experimental factors	<i>γ-Alkynyl 2',3'-dideoxyuridine triphosphate was synthesized and characterized.</i>
Experimental features	<i>A conjugate of the triphosphate with SiO₂ nanoparticle was then obtained by click-chemistry. Chemical stability of the conjugate at different pH values was studied and its cytotoxicity for MCF7 cells analyzed. Experimental details of the synthesis of 2',3'-dideoxyuridine triphosphate conjugated to SiO₂ nanoparticles; data on chemical stability and anti-proliferative activity of the conjugate.</i>
Data source location	<i>Novosibirsk, Russia</i>
Data accessibility	<i>The data are available with this article</i>
Related research article	<i>This data set is submitted as a companion paper to the research article: Svetlana V. Vasilyeva, Inga R. Grin, Boris P. Chelobanov, Dmitry A. Stetsenko. 2',3'-Dideoxyuridine triphosphate conjugated to SiO₂ nanoparticles: synthesis and evaluation of antiproliferative activity. <i>Bioorg Med Chem Lett.</i> 2018; 28:1248, DOI: 10.1016/j.bmcl.2018.02.007.</i>

Value of the data

- The paper relates to the research area of nanoparticle-based biomaterials for biomedical and bioengineering applications.
- This data set presents a protocol for synthesis and characterization of a new bionanoconjugate, which could be used by researchers in the same area.
- The data include a preliminary assessment of antiproliferative properties of a novel conjugate of 2',3'-dideoxyuridine triphosphate with SiO₂ nanoparticles.

1. Data

Data set includes experimental conditions for the synthesis of 2',3'-dideoxyuridine-5'-(N-[4-(prop-2-yn-1-yloxy)butyl]-γ-amino)-triphosphate and its characterization by ¹H, ¹³C, and ³¹P NMR, IR and ESI-MS (Figs. 1–5), and protocol for its click-chemistry conjugation to azido-modified SiO₂ nanoparticles [1,2]. Experimental data on chemical stability of the conjugate at different pH values are presented (Tables 1, 2). Cytotoxicity of the conjugate for MCF7 cell line has been assessed (Table 3).

2. Experimental design, materials, and methods

2.1. Materials and methods

Reagents and solvents were purchased from Sigma-Aldrich or Acros Organics, and used without purification. Aminoalkylated SiO₂ nanoparticles were from SkySpring Nanomaterials (USA). Mass

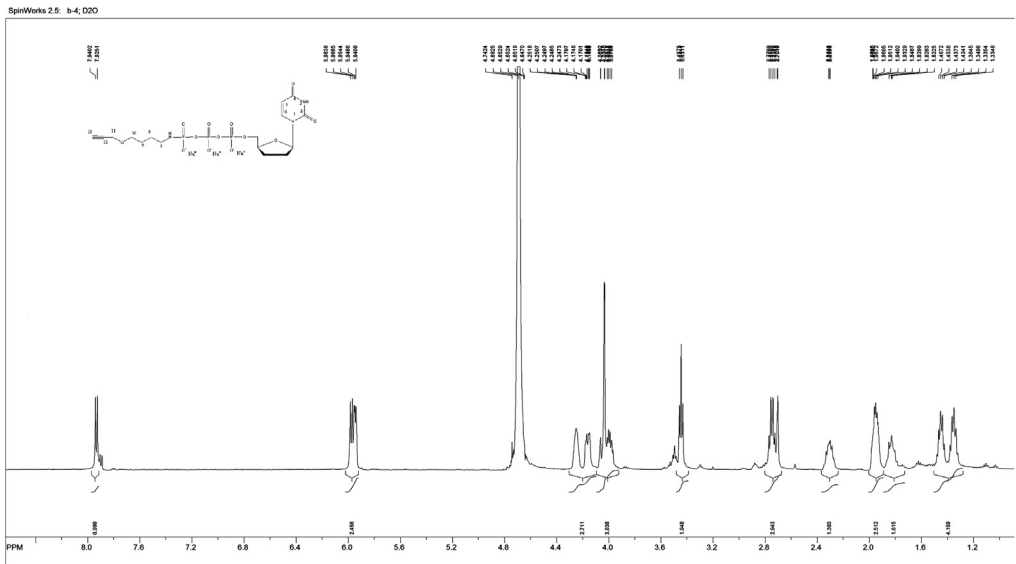


Fig. 1. ^1H NMR spectrum of L~pppddU.

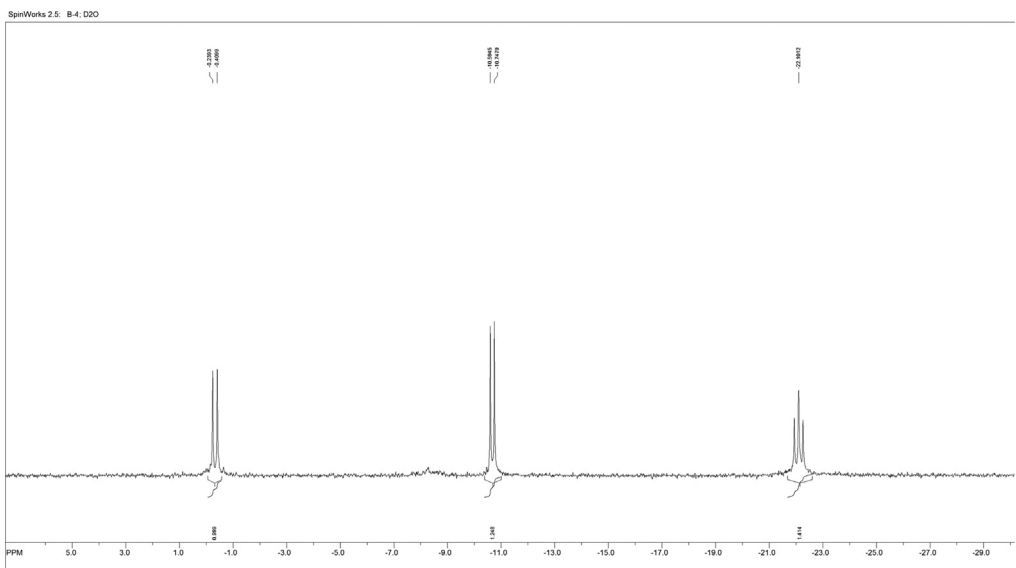


Fig. 2. ^{31}P NMR spectrum of L~pppddU.

spectra were obtained on an Agilent 6410 Triple Quadrupole LC-MS device (USA). ^1H , ^{13}C and ^{31}P NMR spectra were recorded using Bruker AV-400, AV-300 or DRX-500 NMR spectrometers. UV absorption spectra were obtained on a Shimadzu UV-1800 spectrophotometer (Japan). Analytical HPLC was carried out on an Agilent 1200 Series LC system, using Zorbax[®] 5 μm Eclipse-XDB-C18 80 \AA column 150 \times 4.6 mm by Agilent (USA).

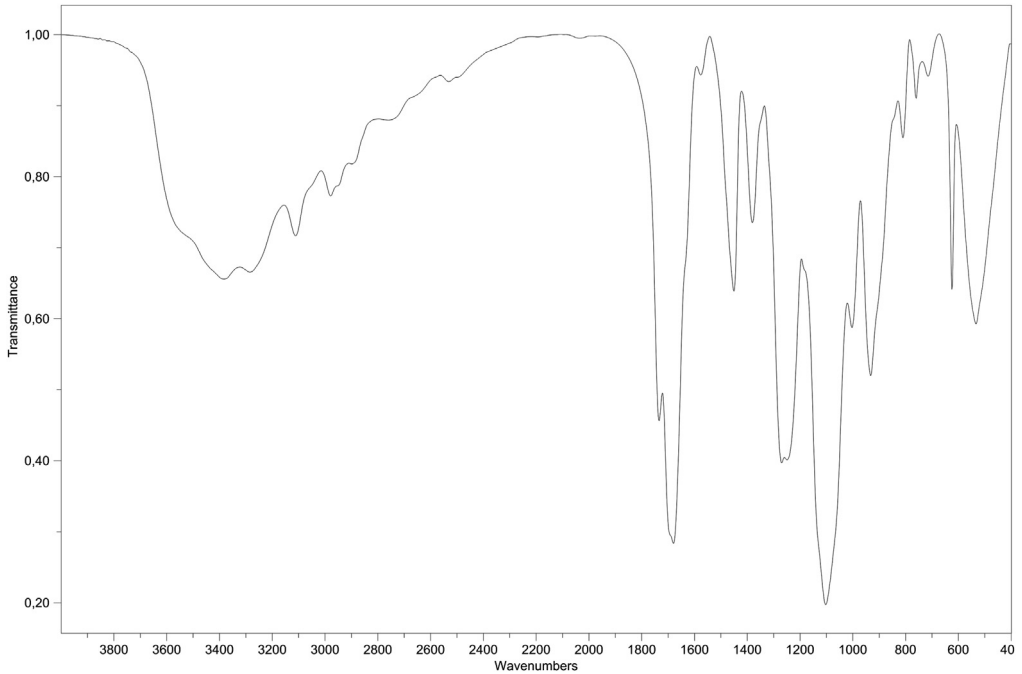


Fig. 5. IR spectrum of L~pppddU.

Table 1

Preparation of sample and control solutions.

No. sample	Compound	Concentration, mM			Nucleotide content ν , $\mu\text{M}/\text{mg}$
		pH 7.3 (PBS)	pH 6.5 (P)	pH 1.5–2 (HCl)	
1	ddU	37.7	28.2	61.2	MW 212.21
2	pppddU	28.8	15.4	34.6	MW 520.27
3	L~pppddU	31.1	44.9	20.0	MW 579.09
5	SiO ₂ ~L*~pppddU	8	8,8	8	0.400

Table 2

Stability of SiO₂~L*~pppddU conjugate and controls at different pH values.

N sample	Sample	Loss of nucleotide content in the sample ^a after 48 h, %			Nucleotide content, ν $\mu\text{M}/\text{mg}$
		pH 7.3 (PBS)	pH 6.5 (P)	pH 1.5–2 (HCl)	
1	ddU	0	0	0	–
2	pppddU	2	0	7	–
3	L~pppddU	9	14	51	–
5	SiO ₂ ~L*~pppddU	36	40	6	0.400

^a Loss of nucleotide content in the samples (1–3) due to decomposition of the controls.

L~pppddU. ¹H NMR (500 MHz, D₂O): δ (ppm) 7.9 (d, 1H, H(6)-(U), $J = 7.7$ Hz); 5.98–5.94 (m, 2H, H(5)-(U), H1'); 4.25–4.17 (m, 2H, H4', H5'); 4.06–3.96 (m, 3H, H5', OCH₂C \equiv CH); 3.44 (t, 2H, OCH₂(CH₂)₃NH, $J = 6.5$ Hz); 2.77–2.70 (m, 3H, O(CH₂)₃CH₂NH, CH \equiv C); 2.34–2.27 (m, 1H, H2');

Table 3IC₅₀ values for MCF7 human breast adenocarcinoma cell line (means ± standard deviations).

Compounds	IC ₅₀ , (MTT),
SiO ₂ ~L*~pppddU	183 ± 57 µg/mL or 22 ± 0.7 µM
SiO ₂ ~L*	no inhibition
ddU	no inhibition
pppddU	no inhibition
L~pppddU	no inhibition

1.97–1.93 (*m*, 3H, H3', 2'); 1.84–1.83 (*m*, 1H, H3'); 1.49–1.32 (*m*, 4H, OCH₂(CH₂)₂CH₂NH). ¹³C NMR (75 MHz, D₂O): δ (ppm) = 164.6 (4-C), 151.6 (2-C), 145.7 (6-C), 103.2 (5-C), 89.8.19 (1'-C), 82.9 (4'-C), 77.9 (12-C), 72.4 (10-C), 68.7 (11-C), 59.7 (5'-C), 57.1 (7-C), 43.6 (2'-C), 33.6 (3'-C), 29.6 (13-C), 26.7 (8-C), 26.6 (9-C). ³¹P NMR (121 MHz, D₂O): δ (ppm) = - 0.3 (*d*, *J* = 20.69 Hz, γ-P), - 10.74 (*d*, *J* = 18.69 Hz, α-P), - 22.10 (*t*, *J* = 20.03 Hz, β-P). UV spectrum (0.2 M NaOH): λ_{max} 260 nm, ε 1883. IR (cm⁻¹): 3360, 3276, 3100, 2973, 2877, 2493, 1660, 1524, 1430, 1385, 1223, 1100, 995, 906, 810, 767. ESI-MS: [M+H-Na]⁺ calcd for C₁₆H₂₄N₃O₁₃P₃Na₂=605.29, found 605.19.

2.3. Synthesis of SiO₂~L*~pppddU and control SiO₂~L* conjugates by CuAAC reaction (Fig. 6)

Azido-modified SiO₂ nanoparticles [2] (40 mg, 17.2 µmol) were sonicated in 200 µL of H₂O. A solution of L~pppddU (100 mM in H₂O, 1.386 mL, 139 µmol, 8 equiv.) was added to the suspension followed by copper(II) sulfate (172 µL of 0.5 M solution in water), 1 M triethylammonium acetate (TEAAc) buffer, pH 7 (172 µL) and sodium ascorbate (86 µL of freshly prepared 1 M solution in water). The reaction mixture was purged with argon for 2 min and stirred at ambient temperature for 12 h. Conjugate was separated by centrifugation, supernatant was discarded. Precipitate was washed successively with 0.1 M NaCl, 10% Na₂EDTA, water, diethyl ether followed by air drying. Yield: 38.5 mg. The control unloaded SiO₂~L*~conjugate was obtained as described above, but without addition of triphosphate. Yield: 9 mg. IR: N₃ group band was absent. The nucleotide content of the conjugate was measured by UV absorbance after dissolving in 0.2 M NaOH. UV spectrum of L~pppddU (0.2 M NaOH): λ_{max} 260 nm, ε 1883. Nucleotide content was calculated as UV absorbance of SiO₂~L*~pppddU conjugate minus UV absorbance of SiO₂~L* conjugate: 0.4 µmol/mg (Fig. 6).

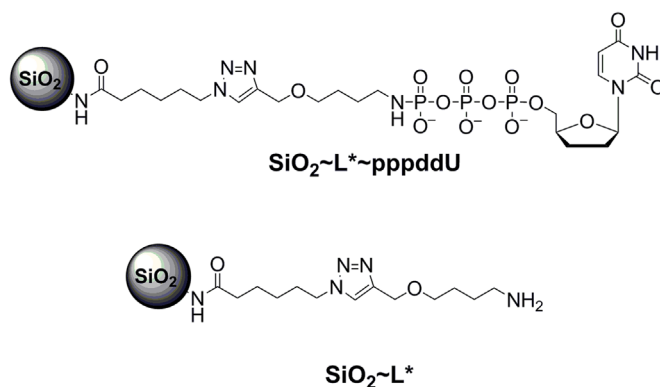


Fig. 6. Structure of the conjugate of 2',3'-dideoxyuridine triphosphate with SiO₂ nanoparticles (SiO₂~L*~pppddU) and control unloaded conjugate (SiO₂~L*).

2.4. Hydrolysis of $\text{SiO}_2\sim\text{L}^*\sim\text{pppddU}$ conjugate at different pH

The conjugate (0.400 $\mu\text{M}/\text{mg}$ nucleotide) was dispersed in three buffers with pH values corresponding to the pH in the blood (pH 7.3), the mouth (pH 6.5) and the stomach (pH 1.5–2.0) (2 mg in 100 μL of each buffer). Parent nucleoside (ddU), its 5'-triphosphate (pppddU) and alkynyl triphosphate ($\text{L}\sim\text{pppddU}$) solutions in the same buffers were prepared (Table 1). The solutions were incubated at 37 °C in a thermomixer. Initial aliquot (15 μL) was taken and analyzed by analytical HPLC at the wavelength 260 nm. Appropriate aliquots of buffers (15 μL) after centrifugation were analysed after 1, 4, 24 and 48 h. Percentage loss of the nucleotide content in the sample of $\text{SiO}_2\sim\text{L}^*\sim\text{pppddU}$ was evaluated at the end of the experiment. The remaining buffers were discarded after centrifugation; conjugate was washed successively with water followed by dissolution in 0.2 M NaOH and UV measurement of the remaining nucleotide content.

2.5. Cytotoxicity assay for human breast adenocarcinoma MCF7 cells

Cells were grown as adherent monolayer cultures in T25 cm^2 culture flasks in complete Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum, 1 mM sodium pyruvate, 2 mM L-glutamine and 1% penicillin-streptomycin-amphotericin B. Cultures were grown at 37 °C under a humidified atmosphere of 5% CO_2 at 37 °C. Cytotoxicity was determined by the colorimetric MTT assay [5]. Cells were harvested from culture flasks by trypsin treatment and seeded in complete medium (100 $\mu\text{L}/\text{well}$) into 96-well plates at 1.5×10^4 cells per well. The cells were allowed to settle and resume proliferation for 24 h. Stock solutions of test compounds were prepared in DMEM, diluted by complete medium and immediately added to the plates (100 $\mu\text{L}/\text{well}$). Control groups with untreated cells were grown under the same condition in complete medium. After 72 h the medium was removed and replaced with 100 $\mu\text{L}/\text{well}$ of 10% MTT solution in complete medium, and the cells were incubated for 3 h at 37 °C. The supernatant was removed, 100 μL of isopropanol was added, and the plates were gently shaken to solubilize the formazan crystals formed. Absorption was measured with a microplate reader (Multiscan EX, Thermo Fisher Scientific, Waltham, MA) at 570 nm and a reference wavelength of 620 nm. The cytotoxicity was expressed as cell growth inhibition (GI) at each group of the cells [6,7]. All samples were analyzed using at least three independent experiments with triplicates for each concentration. The results are shown in Table 3.

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Transparency document. Supplementary material

Transparency data associated with this article can be found in the online version at <https://doi.org/10.1016/j.dib.2018.09.127>.

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