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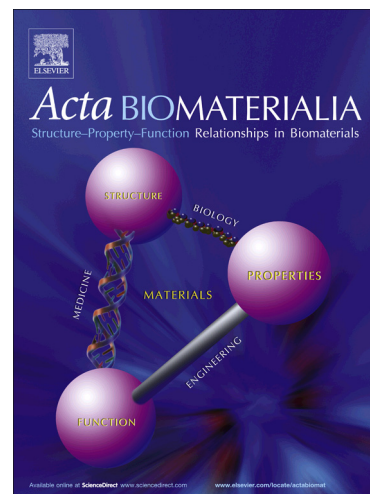
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**Repurposing Disulfiram for Cancer Therapy via Targeted Nanotechnology through Enhanced Tumor Mass Penetration and Disassembly**

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**Abstract:** Disulfiram (DSF), an FDA approved drug for the treatment of alcoholism, degrades to therapeutically active diethyldithiocarbamate (DDTC) in the body by reduction. Hereby, we developed a redox sensitive DDTC-polymer conjugate for targeted cancer therapy. It was found that the DDTC-polymer conjugate modified with a  $\beta$ -D-galactose receptor targeting ligand can self-assemble into LDNP nanoparticle and efficiently enter cancer cells by receptor-mediated endocytosis. Upon cellular uptake, the LDNP nanoparticle degrades and releases DDTC due to the cleavage of disulfide bonds, and subsequently forms copper (II) DDTC complex to kill a broad spectrum of cancer cells. 3D cell culture revealed that this nanoparticle shows much stronger tumor mass penetrating and destructive capacity. Furthermore, LDNP nanoparticles exhibited much greater potency in inhibiting tumor growth in a peritoneal metastatic ovarian tumor model.

**Keywords:** repurpose, disulfiram, cancer, polymer-drug conjugate, nanoparticle

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