

Biodegradable Polymer Drug Delivery Technologies

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1 ▶ Introduction

Polymers have been extensively studied as one of the most promising materials for cancer nanotechnology and cancer drug delivery.¹⁾ It is envisioned that the transfer of nano-engineering capability into cancer chemotherapy will allow drugs to be guided more accurately to tumor cells and to be delivered at a constant concentration to the targeted tumor over a long period of time, minimizing systemic toxicity, and will increase therapeutic efficacy by broadening the range of patients to whom chemotherapy is applicable.²⁾

2 ▶ Innovative Polymeric Cancer Drug Carrier Platform from NDT

Nitto Denko Technical Corporation (NDT) has successfully developed a novel biodegradable polymer drug delivery platform offering a number of unique advantages, including significantly increased carrier solubility and drug-loading capacity combined with carrier stability and good drug-release characteristics, providing a unique scaffold that offers the opportunity to covalently attach a variety of functional molecules with high conjugation density. Based on this platform, the first-generation polymer drug conjugate, NDT-1213, was created by direct conjugation of paclitaxel, the most common anticancer drug for chemotherapy, to an NDT biodegradable polymer. NDT-1213 has been found in various animal tumor models to significantly improve anti-tumor efficacy and dramatically reduce acute systemic toxicity compared to Abraxane (an anticancer drug approved for use in the United States). **Figure 1** presents an example of the anticancer efficacy of NDT-1213.

The increased therapeutic effectiveness of NDT-1213 was a direct result of its improved pharmacokinetic profile. NDT-1213 produced higher levels of drug in the plasma and a marked increase in the amount of drug deposited in the tumor. One of the important advantages of the NDT biodegradable polymer is that it can be loaded with very large amounts of drug, substantially greater than can be achieved with other types of polymer. Another important feature is that, when loaded with paclitaxel, the NDT-1213 carrier spontaneously forms water-soluble nanoparticles of 30-50 nm in size. Such particles are known to accumulate selectively in tumors due to the unusually high vascular porosity of the latter through a phenomenon known as the “enhanced permeability and retention (EPR) effect”. The ability to form nanoparticles contributes importantly to the ability of NDT-1213 to deliver 7.7 times more paclitaxel to the tumor than free drug preparations (**Table 1**).

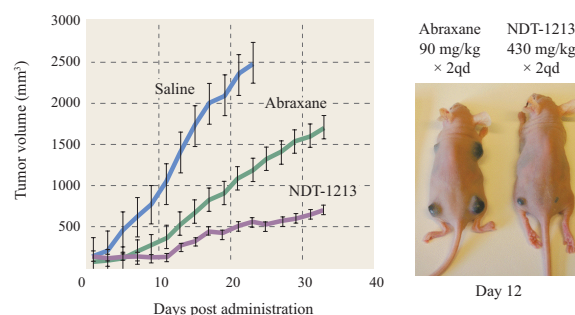
Animal studies show that introducing GRD targeting molecules

or MRI imaging agent into NDT-1213 allows systemic drug distribution to be investigated in real time. In clinical practice, this groundbreaking technology could provide doctors with information on cancer drug distribution and drug efficacy through non-invasive imaging analysis. This is the first known demonstration of a drug carrier system containing both drug delivery and imaging properties.

Cancer treatment represents an enormous biomedical challenge for drug delivery. The NDT biodegradable polymer drug carrier platform is a powerful and flexible drug delivery nanotechnology which holds great promise for: 1) improving the effectiveness of existing therapeutic agents when conjugated to the polymer by selectively enhancing their delivery to the tumor and improving their pharmacokinetic profile; and, 2) offering new opportunities for drugs that have previously failed clinical trials due to high levels of toxicity or poor solubility. Offering targeted and imageable delivery of therapeutic agents to the disease site, the technology has potential in many medical applications in addition to cancer therapy, including neurodegenerative disease, cardiovascular disease, and diabetes.

[References]

1. M. Ferrari, Cancer Nanotechnology: Opportunities and Challenges, *Nat Rev Cancer*, 5(3) p. 161-171 (2005).
2. R. Duncan, Polymer Conjugates as Anticancer Nanomedicines, *Nat Rev Cancer*, 6(9) p. 688-701 (2006).



NDT-1213 was found to have significant anti-tumor efficacy in a B16 melanoma model with lower acute systemic toxicity than Abraxane, the current leading paclitaxel-based drug on the market, which indicates that NDT-1213 delivers more of the drug more safely and without obvious biotoxicity.

Fig. 1 Antitumor growth activity of NDT-1213 versus Abraxane in athymic mice bearing B16 melanoma

Table 1 PK/PD comparison studies: NDT-1213 versus paclitaxel

Plasma (AUC) (h*mg/ml)		Tumor (AUC) (h*mg/ml)	
NDT-1213	Paclitaxel	NDT-1213	Paclitaxel
3.454	0.146	2.496	0.322
NDT-1213/Paclitaxel = 23.6 folds		NDT-1213/Paclitaxel = 7.7 folds	