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Paclitaxel Derivatives and Its Conjugated Bionanoparticles for Targeting Cancer Cells

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As one of the most valuable anticancer agents for a variety of tumors, paclitaxel (**1**) is able to inhibit cell division as well as other interphase processes by stabilizing microtubules. This anticancer agent has extremely low solubility in water. To create a more water-soluble drug for easy formulation, scientists have put enormous efforts on the modification of the paclitaxel structure.

We designed and synthesized new paclitaxel-containing aminophosphates **2a**–**c**,[1] aminoester phosphate **3**, phosphate **4**, and phosphoamidate **5** with better water solubility. These new propaclitaxel analogues were found to possess anti-leukemic activity slightly greater than paclitaxel.

Furthermore, three types of paclitaxel-conjugated nanoparticles (NPs) were synthesized by chemical methods in our laboratory using Fe_3O_4 and Au as the cores. By possessing the polyethylene glycol (PEG)-SH spacer and the phosphate joining unit, the new paclitaxel-P(=O)(OH)-PEG-S-Fe-NP nanomaterials functioned as a prodrug of paclitaxel, which was liberated in the presence of phosphodiesterase. These conjugated nanomaterials constitute a new class of candidates as anti-cancer drugs.[2]

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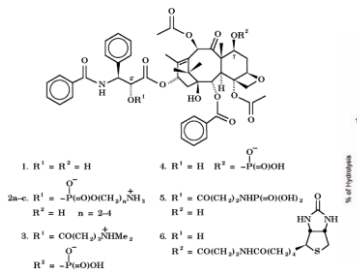

Fig. 1. Derivatives of paclitaxel

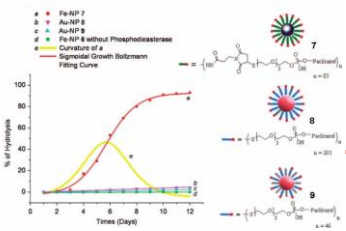

Fig. 2. Hydrolysis of paclitaxel-conjugated NP **7**, **8**, and **9** by phosphodiesterase

1. Sambaiah, T.; King, K.-Y.; Tsay, S.-C.; Mei, N.-W.; Lai, Y.-K.; Lieu, C.-H.; Hwu, J. R. *Eur. J. Med. Chem.* **2002**, *37*, 349.
2. Hwu, J. R.; Lin, Y. S.; Josephrajan, T.; Hsu, M.-H.; Cheng, F.-Y.; Yeh, C.-S.; Su, W.-C.; Shieh, D.-B. *J. Am.Chem. Soc.* **2009**, *131*, 66.

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