

Folic Acid Quenches Doxorubicin Fluorescence

Letter to the Editor

Ghaleb A. Hussein

Chemical Engineering Department, American University of Sharjah, Sharjah, United Arab Emirates

A novel class of nanocarriers in drug delivery is a nanocapsule (a liposome, micelle, solid particle, or vesosome) that is conjugated to a targeting moiety. These targeting molecules are covalently conjugated to the surface of the nanovehicle and include ligands such as folic acid (FA), fibronectin, fibrinogen, herceptin, etc.¹

In this regard, folated drug delivery carriers are of particular interest to researchers namely because of the abundance of folate receptors on the surface of several cell lines/cancerous tissues and the small size of FA molecule (compared to protein targeting moieties). Carriers decorated with FA have been shown to be receptor-mediated endocytosed by several cell lines including KB, HeLa, etc.¹

Most if not all research involving folated micelles and liposomes utilizes fluorescent chemotherapeutic agents and flow cytometry to show an increase in cellular accumulation of the drug encapsulated in the proposed folated carrier. For example, several research articles²⁻⁴ reported the effect of delivering Doxorubicin-Dox (an intrinsically fluorescent anti-neoplastic agent) using targeted micelles or nano-aggregates to folate positive (FR-positive) cell lines. The studies use flow cytometry to quantify Dox accumulation inside MCF-7 and KB cells.

Our experiments with Dox encapsulated in FA-targeted micelles found that flow cytometry underestimates the amount of drug that accumulates inside cells. This conclusion was reached after conducting a fluorescence quenching study in which different concentrations of FA (ranging between 0 $\mu\text{g}/\text{ml}$ and 1.24 $\mu\text{g}/\text{ml}$) were mixed with Dox (final concentration = 5 $\mu\text{g}/\text{ml}$ in phosphate-buffered saline). Dox fluorescence (excitation

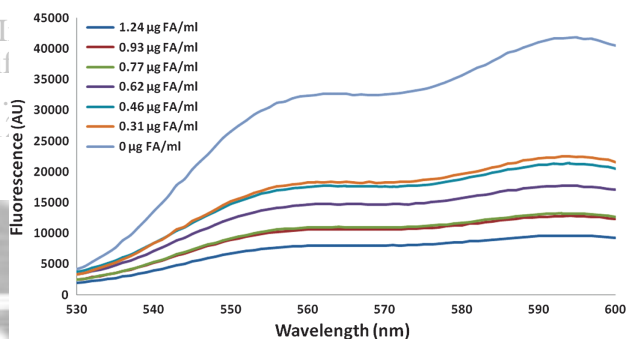


Fig. 1. Average fluorescence ($n = 4$) of Doxorubicin in solutions with different concentrations of folic acid (excitation wavelength = 488 nm).

wavelength = 488 nm, emission wavelength range = 530–600 nm) was then measured using a fluorometer. The results show that folic acid quenches the intrinsic fluorescence of Dox and that the quenching effect increases as the concentration of FA increases (Fig. 1).

Future research using folic acid as a targeting moiety should make the necessary correction when using flow cytometry to compare the accumulation of Doxorubicin.

References and Notes

1. J. Sudimack and R. J. Lee, *Adv. Drug Deliv. Rev.* 41, 147 (2000).
2. E. S. Lee, K. Na, and Y. H. Bae, *J. Control. Release* 103, 405 (2005).
3. H. S. Yoo and T. G. Park, *J. Control. Release* 100, 247 (2004).
4. S. Huang, S. Sun, T. Feng, K. Sung, W. Lui, and L. Wang, *Eur. J. Pharm. Sci.* 38, 64 (2009).

Received: 2 March 2012. Accepted: 5 March 2012.