Design, Synthesis, and Biological Evaluation of Fluorescein-Folic Acid Conjugate As Novel Photosensitizer for Targeted Photodynamic Therapy

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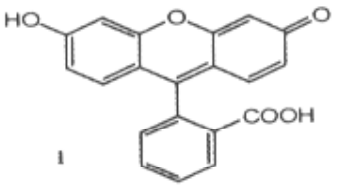
Photodynamic therapy (PDT) is a cancer treatment involving systemic administration of a tumor-localizing photosensitizer; this, when activated by the appropriate light wavelength, interacts with molecular oxygen to form a toxic, short-lived species known as singlet oxygen, which is thought to mediate cellular death. Targeted PDT offers the opportunity of enhancing photodynamic efficiency by directly targeting diseased cells and tissues [1]. Xanthene based dyes such as fluoresceins (**1**) are widely used in sensing applications owing to their brightness, high quantum yields, low-energy excitation and emission wavelengths, and biocompatibility [2]. Recently, a new class of therapeutics based on selective targeting to cancer cells has been developed and grown. Within this growing class of targeted therapeutics, folate-drug conjugates constitute a well studied example of a distinct subclass of receptor targeted therapeutics. Folate selectively binds to and delivers attached conjugates into any cell that expresses a cell surface folate receptor (FR). FR has the ability to transport folate-conjugated therapeutics as well as folic acid (**2**). Once folate-conjugated therapeutics is bound to a cell surface FR, they are transported into the cell through a process called receptor-mediated endocytosis [3].

With this application in mind, a variety of folate-linked molecules and complexes have been designed to enable selective delivery of drugs to FR+ cancer cells. Considering all stated above, a new conjugate of fluoresceine-folic acid was synthesized. The conjugate was characterized by ^{1}H-NMR, IR, UV-vis spectroscopy, and fluorescence quantum yield.



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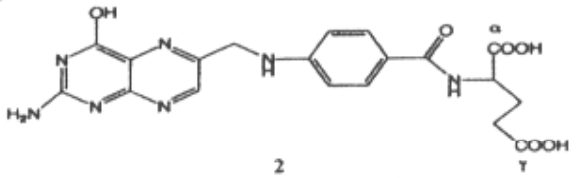

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Reference

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2. Nalan, E. M; Burdette, S. C.; Harvey, J. H. *Inorg. Chem.*2004, *43*, 2624.
3. Schneider, R.; Schmitt, F.; Frochot, C.; Fort, Y.; Lourette, N.; Guillemin, F.; Muller, J.-F.; Barberi-Heyob, M. M. *Bioorg. Med. Chem.* 2005, *13*, 2799.