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Labeling of Fluorescein Dye on Folate Binding Protein

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Labeling of Fluorescein Dye on Folate Binding Protein.

A Project

Submitted

To

Governors State University

By

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In Partial Fulfillment of the

Requirements for the Degree

Of

Masters in Analytical Chemistry

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Abstract:

Discovery and development of folic acid based receptor targeting started in late 1991 and early 1992 when researchers came to know that folate receptors (FR) are over expressed on malignant tissues¹. The malignant tissues over express special folate receptors to capture more folate from the blood stream as folate is required for cell division^{1,2}. The researchers found that folate can be used as an optimal targeting ligand that would bind selectively to pathologic cells, displaying no affinity for healthy cells. Then they focused on attaching a drug molecule to the folate ligand that can be delivered directly to the cells which led to the discovery of tumor-selective drug delivery system. In tumor-selective drug delivery folic acid till date has been linked to (i) protein toxins, (ii) chemotherapeutic agents, (iii) gene therapy vectors, (iv) oligonucleotides (including small interfering RNA (siRNA)), (v) radioimaging agents, (vi) magnetic resonance imaging (MRI) contrast agents, (vii) liposomes with entrapped drugs, (viii) radiotherapeutic agents, (ix) immunotherapeutic agents, and (x) enzyme constructs for prodrug therapy.¹⁻³ Further research on developing folate-conjugated drugs led to the discovery of, over expression of folate receptors on activated macrophages which either cause or contribute to diseases such as rheumatoid arthritis, Crohn's disease, atherosclerosis, lupus, inflammatory osteoarthritis^{1,3,4}. There was a significant concern that healthy tissues might be targeted with folate drug conjugates and the most efficient method for assessing was to examine the biodistribution of radio labeled and dye labeled folate-linked imaging agents.¹⁻³

As an above motive, we developed low cost and simple procedures for the synthesis and analytical analysis of fluorescent dye labeled folate-protein conjugate. This method should find tremendous use in *vitro* and *in vivo* studies of fluorescent labeling on protein conjugates and imaging the biodistribution of dye labeled folate conjugates.