ENHANCEMENT OF PROTOPORPHYRIN IX ACCUMULATION BY ALGINATE-INCORPORATED AND FOLIC ACID-CONJUGATED CHITOSAN NANO-PARTICLES FOR COLORECTAL CANCER PHOTODYNAMIC DETECTION

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Introduction. The incidence of colorectal cancer is increasing worldwide and its prognosis remains poor. In general, survival is inversely related to extent of tumor spread at time of detection. Relative rates of survival of 50 % at three years and 40 % at five years have remained unchanged since the 1960s. Prognosis is excellent with detection at an early stage. Unfortunately, small colorectal neoplasia and early cancer are frequently overlooked during endoscopy. Therefore, a powerful and highly-sensitive tool for the detection of precancerous lesions would be of great value.
Background. Photo-diagnosis is one of the most promising and non-invasive methods for detecting malignant or premalignant tissue. Currently, detection of abnormal tissue usually involves the use of an exogenous chromophore, such as protoporphyrin IX (PpIX), excited by optima light to generate fluorescence in cancer lesions. The 5-aminolevulinic acid used in the study, a precursor in heme group synthesis, is totally degraded intracellularly and converted to PpIX. Because the decomposition rate of PpIX in cancer cells differs from that in normal cells, the photosensitive fluorophore, PpIX, can be used to detect cancer lesions.
Purpose: We aimed to synthesize an alginate-incorporated and folic acid-conjugated chitosan nano-particle as a suitable vehicle for carrying 5-aminolaevulinic acid (5-ALA) to enhance the detection of colorectal cancer in vivo after a short-term uptake period.
Methods. Chitosan was successfully conjugated with folic acid to produce folic acid-chitosan conjugate, which was then loaded with 5-ALA and incorporated with alginate to create nano-particles (fCANA). The fCANA was then incubated with HT-29 colorectal cancer cell line to determine the rate of accumulation of protoporphyrin IX (PpIX). Average particle size, zeta-potential, and loading efficiency of 5-ALA in fCANA were also measured.
Results. The loading efficiency of 5-ALA in fCANA particles and the average size were 26.7% and 116 nm, respectively. The zeta-potential of fCANA was 21.8 mV, enough to keep the nano-particle stable without aggregation. The fCANA could be taken up easily by HT-29 cell line after short-term uptake period, most likely via receptor-mediated endocytosis and electrostatic attraction. Moreover, the PpIX accumulation could be improved by fCANA in comparison with fCNA, suggesting that the 5-ALA release from the prepared fCANA could be enhanced due to the competition of the negatively charged alginate to the positively charged chitosan, and then converted to PpIX in colorectal cancer cells.
Conclusion. The use of alginate and folic acid-chitosan conjugate appears to be an ideal vector for colorectal-specific delivery of 5-ALA for fluorescent endoscopic detection.

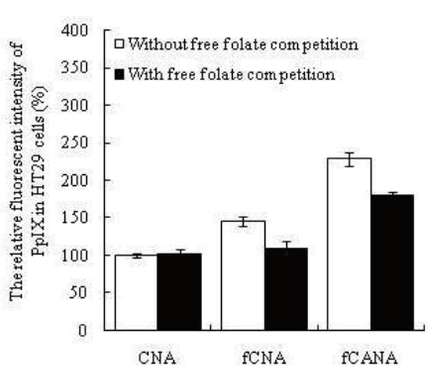

Figure 1. The relative PpIX concentration in HT29 cells after fed with CNA, fCNA and fCANA for 12 hours. The brightness of the emission light of the CNA group was designated as 100%.