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Extended Abstract

Chemically Modified Hemocyanins with Enhanced Antibreast Cancer Activities †

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Some cancer cells hyperexpress folate receptors (FR); therefore, folate-derivatized delivery systems are applied for a selective delivery of chemotherapeutics. Recent reports have shown that folate-conjugated immunoglobulin induce an immune response from NK cells against FR-positive melanoma tumor cells [1]. Hemocyanins (Hcs) are respiratory copper-containing glycoproteins that present in the hemolymph of arthropods and mollusks. Numerous studies have shown that Hcs induce a potent Th1-dominant immune response when used as a drug carrier or vaccine adjuvant and nonspecific immunostimulant in cancer or have potential as antineoplastic agents [2].

The aim of this pilot study is to obtain potent and selective anticancer agents based on Hcs isolated from marine snails *Rapana thomasiana* (RtH) and from garden snails *Helix lucorum* (HlH). The proteins were conjugated with folic acid (FO) and ferulic acid (FE) in two-step reactions that involve formation of active N-hydroxysuccinimide folates and ferulates and their subsequent covalent bonding to the Hcs. RtH and HlH conjugates with a different degree of FO and FE substitution were obtained and purified by gel filtration chromatography. Using ATR-FTIR spectroscopy, we observed significant conformational changes in Hc molecules which are ascribed to the chemical modification. Interestingly, the DSC experiments have shown that the thermal stability of all proteins was preserved. RtH-FO, RtH-FE, HlH-FO, and HlH-FE are not cytotoxic to human fibroblasts (BJ cells) even if applied at concentrations as high as 2 mg/mL. The four preparations exhibit an excellent cytotoxic effect to hormone-dependent MCF-7 and hormone-independent triple-negative MDA-MB-231 breast cancer cells, and their selectivity varies within the tested proteins.

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References

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