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Abstract

Photodynamic therapy (PDT) exploits light interactions and photosensitizers to induce cytotoxic reactive oxygen species [1, 2]. Photodynamic diagnosis (PDD) uses the phenomenon of photosensitizer emitting fluorescence to distinguish some tumors from normal tissue. The standard photosensitizer used for PDD is 5-aminolevulinic acid (5-ALA), although it is not entirely satisfactory[3-7]. We previously reported glucose-conjugated chlorin (G-chlorin) as a more effective photosensitizer than another widely used photosensitizer, talaporfin sodium (TS); however, G-chlorin is hydrophobic [8, 9]. We synthesized oligosaccharide-conjugated chlorin (O-chlorin) with improved water-solubility. We report herein on its accumulation and cytotoxicity.

O-chlorin was synthesized and examined for solubility. Flow cytometric analysis was performed to evaluate O-chlorin accumulation in cancer cells. To evaluate the intracellular localization of photosensitizer, cells were stained with O-chlorin and organelle-specific fluorescent probes. We then measured the *in vitro* fluorescence of various photosensitizers and the half-maximal inhibitory concentrations to evaluate effects in PDD and PDT, respectively. Xenograft tumor models were established, and antitumor and visibility effects were analyzed.

O-chlorin was first shown to be hydrophilic. Flow cytometry then revealed a 20- to

40-times higher accumulation of O-chlorin in cancer cells than of TS, and a 7- to 23-times greater fluorescence than 5-ALA. *In vitro*, the cytotoxicity of O-chlorin PDT was stronger than that of TS PDT, and O-chlorin tended to accumulate in lysosomes. *In vivo*, O-chlorin showed the best effect in PDT and PDD compared to other photosensitizers.

O-chlorin was hydrophilic and showed excellent tumor accumulation and fluorescence. O-chlorin is promising as a next-generation bifunctional photosensitizer candidate for both PDT and PDD.

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