Synthesis of polyimide dendric phthalocyanines and their biochemical properties

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Introduction

Phthalcyanines possess a similar structure to porphyrin such as hemoglobin, chlorophyll, cytichrome P450 and vitamin B12. Then, phthalocyanines have been utilized in important functional materials. Especially, aluminum and zinc phthalocyanins are expected to utilize as a next generation photosensitizer for photodynamic therapy of cancer (PDT) [1-3].

Phthalocyanines as PDT photosensitizer accumulated in cancer cells are attack to destroy damaging cells, which had received enough light to produce lethal amounts of singlet oxygen. The sensitizer for PDT requires a high photostability, high selectivity to tumors, no cytotoxity when no light is irradiated, strong absorption in the region between 600 and 800 nm where penetration of tissue is good, and a long triplet state lifetime [4].

Phthalocyanines for PDT photosensitizer have attracted attention as formation of nano-scale ordered architecture existing in nature world. In order to construct nano-scale ordered architecture, novel photosensitizer was proposed dendric phthalocyanines, which possesses polyimide dendritic parts as side chains and carbokylc phthalocyanine as core parts. The polyimido dendric parts of dendritic phthalocyanine expect functions for photo-antenna and genetic vector.

Dendrons and/or dendrimers are hyperbranched constitutions to make nano-scale ball shape molecule, and the functions such as photo-antenna and genetic vector based on their form. On the other hand, functions of phthalocyanines carry on their central metals. Then, if dendritic parts covered with the central metal, the phthalocyanine core is inhibited to display the function of PDT photosensitizer.

In this study, we molecular-designed and attempt to syntheses novel donuts shape zinc polyamido phthalocyanine dendrons which possessed low-generation polyimido dendoron having either biological affinity and photo-antenna ability or inhibition of PDT efficacy. Synthesis of the dendrotic part of novel donuts shape zinc polyimido phthalocyanine dendrons was used for convergent method. The core part of them was then adopted zinc phthalocyanine poly(carboxylic acids).

The novel donuts shape zinc zinc polyimido dendric phthalocyanine were evaluated their PDT efficacy by cancer cell culture.

Results and Discussion

Dendron synthesis was to use a simple and symmetrical monomer, which was chosen as \(N\text{-}(\text{tert-butoxycarbonyl})\text{iminodipropionic acid}\). Starting material having two functional groups as carboxylic acid was available for the condensation step. \(N\text{-}(\text{tert-butoxycarbonyl})\text{iminodipropionic acid}\) was synthesized in two steps: hydrolysis of 3,3'-iminodipropionitrile with hydrochloric acid gave the 3, 3'-iminodipropionitrile with hydrochloric acid gave the 3, 3'-iminodipropionic acid which was protected using di-tert-buthyl dicarbonate (Boc) to give \(N\text{-}(\text{tert-Boc})\text{iminodipropionic acid}\) in 11% yield.

Core part of zinc polyimindo dendritic phthalocyanines was adopted two types of zinc phthalocyanine poly(carboxylic acids). The phthalocyanines were synthesized in accordance with

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Wyler’s method using phthalic derivative and urea. Type 1 zinc phthalocyanine poly(carboxylic acids) were synthesized from 4-carboxylic phthalic anhydride (trimellic anhydride), phthalic anhydride, zinc chloride, and urea. Type 2 zinc phthalocyanine poly(carboxylic acids) were synthesized in accordance with literature methods [5], and from benzene-1,2,4,5-tetra carboxylic dianhydride (pyromellitic dianhydride), phthalic anhydride, zinc chloride, and urea.

Zinc polyimido dendric phthalocyanine dendorons having Type 1 were synthesized with Type 1 zinc phthalocyanine poly(carboxylic acids), and G1, G 1.5 or G2 dendrons (Scheme 1).

Type 2 dendrons were synthesized in much the same way as Type 1 dendrons (Schem 2). As both Type 1 and 2 dendron, Q bands appeared around 690 nm and fluorescence maxima showed approximately 715 nm.

Interaction between zinc poly(aminoamine) phthalocyanine dendrons and cancer cell

The uptake of zinc polyimido dendritic phthalocyanine was done in IU-002 cells. IU-002 cells were incubated with various concentrations of zinc polyimido dendritic phthalocyanine at 37°C. After incubation for 3h, zinc zinc polyimido dendric phthalocyanine concentration were measured. Cellular zinc zinc polyimido dendric phthalocyanine uptake increased with phthalocyanine dendron concentration.

In general phthalocyanines easily aggregate and aggregated phthalocyanines do not act as a photosensitizer [5]. It is known that the aggregated phthalocyanines are not fluorescent.

Zinc zinc polyimido dendric phthalocyanine in IU-002 cells exhibited the fluorescence in the cells.

Fig.3 Photocytoxity of Zinc polyimido dendric phthalocyanine. In the case of Type 1 type G1 mono polyimido dendric phthalocyanine.

After cells uptake Type 1 type G1 mono polyimido dendritic phthalocyanine, Type 1 type G1 tetra polyimido dendric phthalocyanine, Type 2 type G1 octa poly(aminoamine)phthalocyanine dendron and Type 2 type G1.5 octa polyimido dendric phthalocyanine, respectivey were exposed halogen light for 10 minutes, lethal cells increased with increasing zinc polyimido dendric phthalocyanine concentration (Fig. 1). On the other hand, lethal cells were not increased without irradiation.

These results means that zinc polyimido dendric phthalocyanine have highly photodynamic damage to cells.

References