Development of charged liposomal delivery system for enhanced algicidal effect of DP-92

Yu Jin Cho, Jun-Pil Jee *

College of Pharmacy, Chosun University, Gwangju 501-759, Republic of Korea

A R T I C L E   I N F O

Article history:
Available online 25 November 2015

Keywords:
Harmful algae
Liposome
Algicidal activity
Delivery system

Harmful algal blooms (HABs) known as red tides have brought serious problems in marine environments and aquaculture industries, and have threatened marine organisms and human health. Several methods have been studied to treat HABs such as clay flocculants, bioresources and chemical algicides. Although the usage of chemical algicides is the most common method for the management of HABs effects, the undesirable toxicity and economical cost limit the wide application of chemical algicides [1].

We have chemically synthesized series of thiazolidinedione (TD) derivatives to manage the HABs. The TD derivatives exhibited remarkable algicidal effect on HABs, especially green tide, however, did not exhibit the effect on red tide. To treat red tide, new algicidal agent, N-[(3,4-dichlorophenyl)methyl]cyclohexanamine (DP-92), was synthesized. DP-92 induced a high degree of selective algicidal effect on red tide. However, DP-92 was not soluble in aqueous solution and improvement of its solubility was needed to enhance its algicidal effect and wide application in marine environment [2,3].

In order to improve algicidal effect of DP-92, we designed the charged liposomal delivery system for DP-92 and evaluated the algicidal effects of DP-92 loaded liposomal delivery systems.

Liposomes were prepared with phospholipids, cholesterol and algicidal agent DP-92. L-α-phosphatidylcholine (EggPC), 1,2-di-(9Z-octadecenoyl)-sn-glycero-3-phosphocholine (DOPC) or 1,2-di-(9Z-octadecenoyl)-3-trimethylammonium-propane chloride salt (DOTAP) was employed to prepare different surface-charged liposomes. The properties of liposomes were characterized such as mean diameter, zeta potential and encapsulation efficiency (EE%). To evaluate the algicidal effect of the charged liposomes, Heterosigma akashiwo (H. akashiwo), a type of red tide, was exposed to DP-92 loaded liposomes at final DP-92 concentrations of 0.05, 0.1, 0.2, 0.4, 0.5 and 1 μM for 24 h, and IC50 value was calculated. Mean diameter of the liposomes composed of Egg PC, DOPC and DOTAP were 179.4 ± 0.3, 136.7 ± 0.09 and 166.6 ± 0.22 nm, respectively, and their zeta potential value were −32.5 ± 0.8, −5.7 ± 0.5 and +25.6 ± 1.2 mV, respectively. EE% values of the liposomes were 95, 95 and 98%, respectively. IC50 values of DP-92 in liposomes against H. akashiwo were lower than that of free DP-92 in DMSO (0.62 μM). Especially, DP-92 in positively charged liposome had the lowest IC50 value as 0.51 μM. The charge–charge...
interaction between the positively charged surface of the liposomes and the negatively charged wall of *H. akashiwo* results in more efficient delivery of DP-92 to *H. akashiwo* and higher algicidal effect compared to those of neutral or negatively charged liposome.

In conclusion, the positively charged liposomal delivery system for DP-92 appeared to be effective to enhance the efficacy of DP-92 and showed great potential as an effective tool for treatment of HABs.

**REFERENCES**

