New photosensitizers for the photodynamic inactivation of Gram positive and Gram negative bacteria

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Abstract

The efficiency of sulfonamide-substituted phthalocyanines in the PDI of Gram negative and Gram positive bacteria was evaluated. Zinc phthalocyanines bearing simple sulfonamide units (N,N-diethylsulfonamide, N-isopropylsulfonamide, or N-4-methoxyphenylsulfonamide) caused stronger inactivation than phthalocyanines bearing heterocyclic structures (N-thiazol-3-ylsulfonamide) or long chains (N-dodecylsulfonamide), in both bacteria. Furthermore, the encapsulation of these compounds within PVP polymeric micelles, used as drug delivery vehicle, enhanced the inactivation efficiency. The results show that these encapsulated compounds are a promising class of photosensitizers to be used in PDI.

Introduction

Phthalocyanines (Pcs) are highly blue-green colored macrocycles that, while having a similar structure to natural porphyrins, are not found in Nature. Due to their structural and photophysical properties, Pcs are currently used (or are potentially useful) in a range of scientific areas. In particular, they have been intensively studied as photosensitizers in the photodynamic therapy of tumors (PDT) and in the photodynamic inactivation of microorganisms (PDI).

The functionalization of the periphery of Pcs allows to modulate their properties or to provide compounds with new potentialities. The insertion of sulfonamide groups at the phthalocyanine periphery is an example of such transformations. In recent years sulfonamides have been studied as inhibitors and activators of different enzymes in several biological systems. Their most known biological activity is as antimicrobials by the inhibition of the enzyme dihydropteroate synthase in the folic acid pathway.

In this communication we report the successful PDI of Escherichia coli and Staphylococcus aureus using Pcs bearing four or eight sulfonamide groups (Scheme 1), either in solution or encapsulated in a PVP micelle, as photosensitizers (PSs).

Results and discussion

The encapsulation of the synthesized phthalocyanines in the drug delivery vehicle (PVP), intended to improve the solubility of the Pcs in aqueous media, was a successful strategy by an increase of solubility and in singlet oxygen generation when compared with Pcs in solution. This property is due to the accommodation of the Pcs within polymer micelles in the monomeric state, confirming that the encapsulation in PVP strongly improves the solubility of these Pcs in aqueous media.

In vitro assays were performed to appraise their potential as PSs for the inactivation under white and red light (Figure 1) of E. coli (Table 1) and S. aureus (Table 2).

Conclusion

The experimental results demonstrated the efficient photoinactivation of E. coli and S. aureus (used as Gram negative and Gram positive bacterial models) by Pcs bearing sulfonamide units. A comparative analysis of the performance of the free and the PVP-encapsulated forms of sulfonamide-substituted Pcs was also established, highlighting a PVP monomerization effect that enhance singlet oxygen generation and consequently improves the efficiency of inactivation. Pcs Zn1, Zn2, Zn4 and Zn6 stand out as particularly promising photosensitizers.

This work opens a new window for the study of phthalocyanines bearing sulfonamide units as photosensitizers: a synergic effect of the phthalocyanine properties and the biocidal properties of sulfonamides is probably occurring. It also acts as a new strategy against antibiotics resistance.

References


