

Review

Functionality stored in the structures of cyclodextrin–porphyrinoid systems



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ARTICLE INFO

Article history:

Received 15 February 2015

Accepted 29 April 2015

Available online 8 May 2015

Keywords:

Biomimetics

Drug delivery systems

Hemoglobin mimicking

Inclusion complexes

Light harvesting

Photodynamic therapy

ABSTRACT

The binding of cyclodextrins and porphyrinoids (including porphyrins, phthalocyanines and chlorins) is carried out by both covalent linking or inclusion complexation. Many of the resulting structures possess intrinsic biomimetic functionality. Therefore, they have been investigated as biomimetics, which imitate some biochemical processes occurring in nature, such as carotene cleavage, cytochrome P450-mediated hydroxylation, oxygen binding by hemoglobin, or as components of multichromophoric arrays in light harvesting antenna systems. Interestingly enough, cyclodextrins improve porphyrinoids photosensitizing properties by increasing the values of singlet oxygen generation quantum yield which is of immense value for applications in photodynamic therapy. Noteworthy is the great potential for medical applications, revealed recently in the construction of sophisticated systems consisting of covalently linked cyclodextrins and photosensitizers that were considered as carriers for multimodal anticancer therapy.

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Abbreviations: AFM, atomic force microscope; CD, cyclodextrin; DOTAP, N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride; GPx, glutathione peroxidase; IC₅₀, half maximal inhibitory concentration; IgG, immunoglobulin G; K, binding constant; MRSA, methicillin-resistant *Staphylococcus aureus*; PDT, photodynamic therapy; PEG, polyethylene glycol; PhIO, iodosobenzene; PNIPAAm, poly(N-isopropylacrylamide); PM-β-CD, permethylated-β-cyclodextrin; ROS, reactive oxygen species; S, spin quantum number; SMPM, supramolecular polymer micelle; SOD, superoxide dismutase; STM, scanning tunneling microscopy; TEM, transmission electron microscopy; THPP, tetrakis(4-hydroxyphenyl)porphyrin; TPPS, tetrakis(4-sulfonatophenyl)porphyrin.

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<http://dx.doi.org/10.1016/j.ccr.2015.04.009>

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1. Introduction

Supramolecular chemistry is used to develop molecules which can be applied as building blocks to construct systems showing novel, intriguing properties, different from those of their single components. Supramolecular systems often resemble naturally occurring molecules in structure and function, and, therefore, they are examined as biomimetics. Key life processes, like photosynthesis, or oxygen storage are dependent on complex, supramolecular building molecules, including porphyrinoids (Scheme 1).

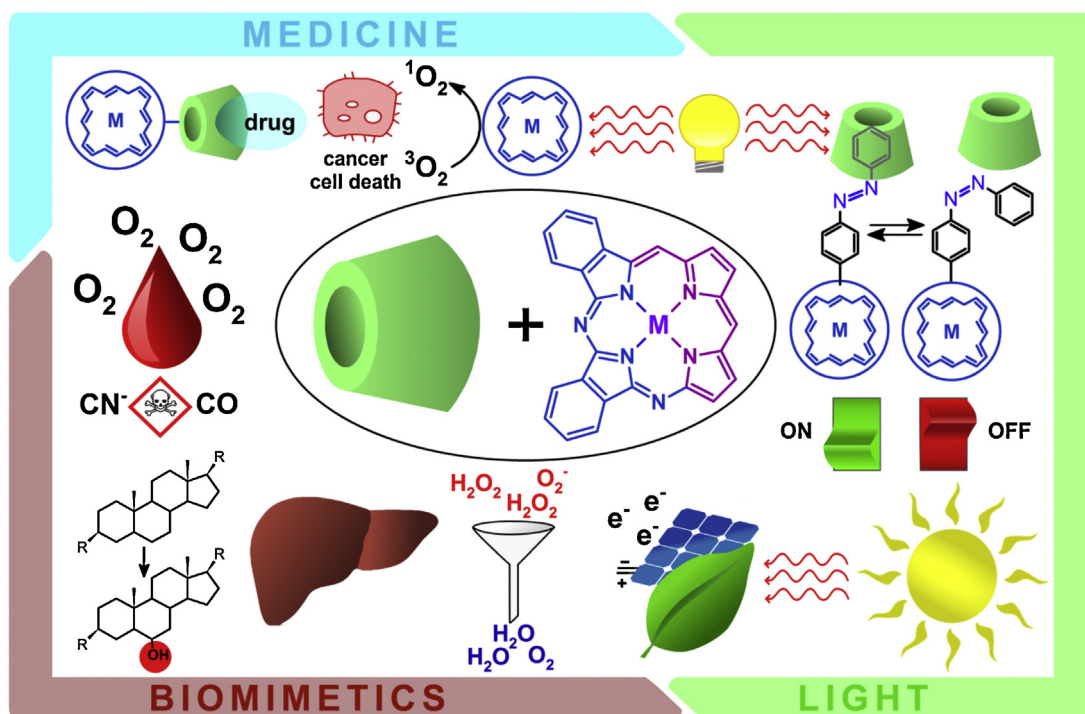
Both cyclodextrins (CDs) and porphyrinoids have been widely examined, separately and jointly, for applications in supramolecular chemistry, which paved the way to the molecular systems, showing properties inaccessible by other means.

Native cyclodextrins (CDs) are cyclic oligosaccharides consisting of 6, 7, or 8 D-glucopyranose units bound together by a α -1,4-glycosidic linkage, and referred to as α -, β -, or γ -CD, respectively (Fig. 1). These toroidal-shaped molecules have inner hydrophobic cavities, lined with C–H groups and glycosidic oxygen bridges and an external hydrophilic surface covered with hydroxyl groups. Hydrophobic cavities provide a unique opportunity to assembly host–guest complexes. Furthermore, the CDs have been considered as carriers for poorly water-soluble drugs in pharmaceutical technology [1–3]. In addition, several attempts have been made to selectively modify the primary and secondary hydroxyl groups in CDs and study their biomimetic activity as the hydrophobic cavity resembles the enzyme active sites [4]. Studies involving CD derivatives bearing bridging caps (units that bridge CD entrance) in terms of guest complexation, catalytic activity, and photochemistry, have been discussed by Engeldinger et al. [5]. Therein referenced research on CD–porphyrin conjugates comprises mainly the data obtained by the Yasuhisa Kuroda group from the Kyoto University which are discussed in the next Sections 2.1 and 4 of this review. Noteworthy, Ronald Breslow has described widely artificial enzymes [6], many of which are CDs bearing additional groups.

Porphyrins are the macrocycles consisting of four pyrrole rings and substituted at the peripheral β and interpyrrolic (meso,

methine) positions (Fig. 1). Porphyrin derivatives, unlike the parent porphyrin heterocycles, are soluble in common solvents and are similar to naturally occurring compounds. Of biochemical significance are chlorins, which are dihydro derivatives of porphyrins. The macrocyclic core of porphyrin systems is planar and highly conjugated with nominally 22π -electrons of which 18 are included in a conjugative path. Porphyrin analogs, chlorins have 18π -electrons engaged in delocalization system, but the number of resonance forms is reduced in comparison to that of porphyrins. The chelation process of the inner two NH protons with metal ions leads to metal chelates. Chlorophyll, a natural component of plant photosystems is a derivative of chlorin. Most porphyrin and chlorin derivatives show biochemical functions only in the form of metal complexes, e.g. iron(II) in hemoglobins, magnesium(II) in chlorophylls. The cobalt corrinoids are obtained biosynthetically from uroporphyrinogen III. The tetrapyrrolic ring of corrole macrocycle consists of 19 carbon atoms, whereas porphyrins and chlorins possess 20 carbon atoms in their cores. Another characteristic feature of corroles is the lack of a methine bridge between the A and D pyrrole rings. Corroles are aromatic macrocycles with 18π -electrons included in the conjugation and carry three NH protons, while corrins are not aromatic and contain only one NH proton. The key natural product with the corrin ring is cobalamin (vitamin B₁₂). Phthalocyanines are tetrabenzotetraazaporphyrins and they can have substituents at peripheral (α) and non-peripheral (β) positions of the four benzene rings. As compared to the porphyrin ring, they have meso nitrogen atoms and fused benzo-rings. They are extremely photostable and insoluble in most solvents. They can be considered as models of hemes and chlorophylls. Their significance lies, for the most part, in the fact that they can be applied as dyestuffs. Nevertheless, the importance of phthalocyanines in medicine and technology is increasing [7–11].

Over the last century, there has been a growing interest in natural porphyrinoids, which play a key role in the structures responsible for the various vital functions, including oxygen binding (heme in hemoglobin and myoglobin), electron transport chain (cytochrome c oxidase), metabolism (cytochrome P450)



Scheme 1. Various functionalities of cyclodextrin–porphyrinoid systems.

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