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Isoporphyrins – Bioinspired NIR-Dyes

A contemporary concept in cancer therapy relies on the use of light and oxygen for cancer cell destruction. This process called *Photodynamic Therapy*, or shortly PDT, is mediated by suitable dyes, which are applied locally to the malignant tissue. Once in place, these dyes collect light and transform the light energy to activate abundant oxygen. Activated oxygen species then attack the cancer cell (Fig. 1).

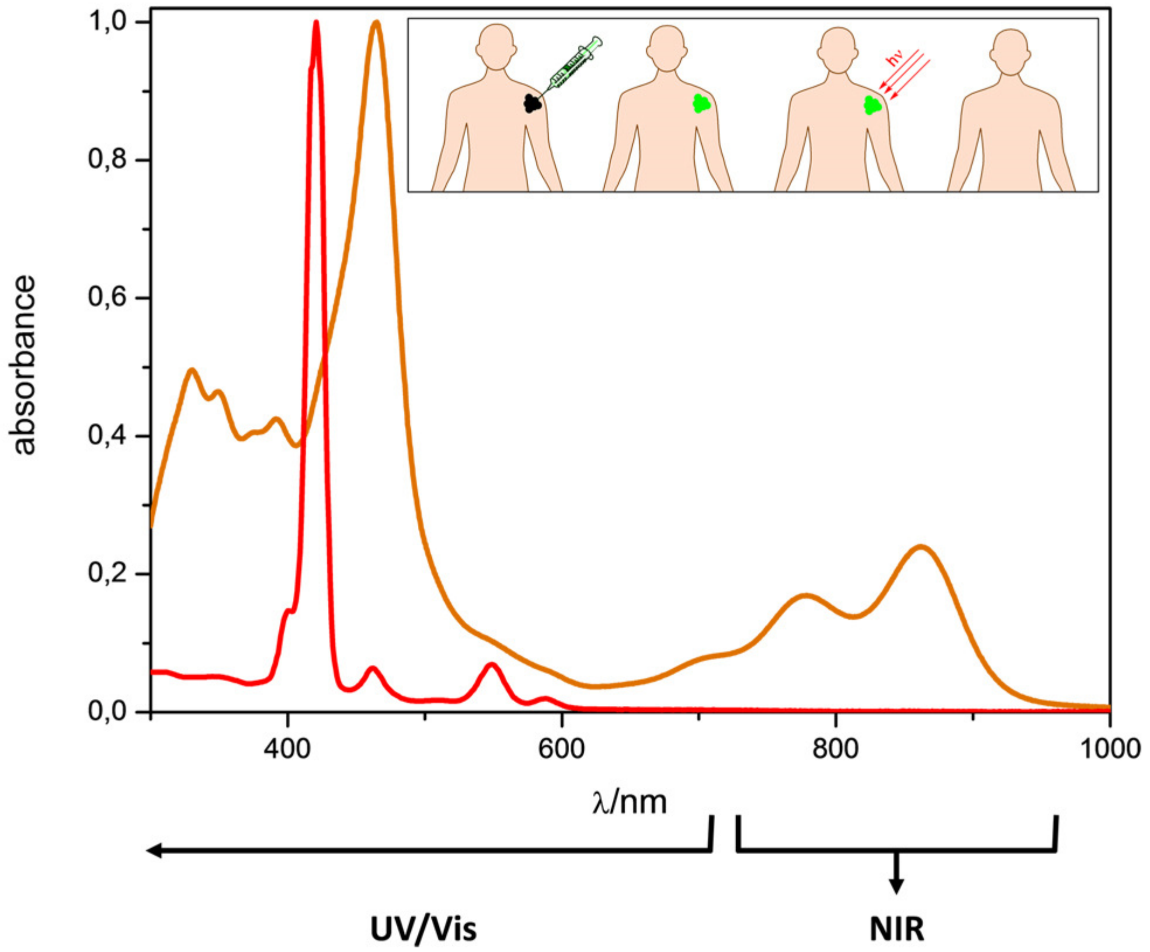

Fig. 1. UV/Vis absorption spectra of zinc isoporphyrin (brown) and zinc porphyrin (red). The inset details the process of photodynamic therapy (PDT).

The human body contains a large number of such PDT suitable dyes as prosthetic groups in many enzymes, of which the oxygen transporter protein of our blood, *haemoglobin*, is the most prominent example. These dyes are called *hemes*, and they chemically belong to the class of metal porphyrins (Fig. 2). Derivatives of these ubiquitous *hemes* have a long-standing history in PDT research (“Photofrin”). However, such heme-derived dyes absorb light of similar energies as the natural archetype, which leads to two major drawbacks.

First, only little specificity can be reached for targeting the cancer cells, and second, most of the applied light is already absorbed within the first milimeters of healthy tissue by natural hemes, and it never reaches the site of action.

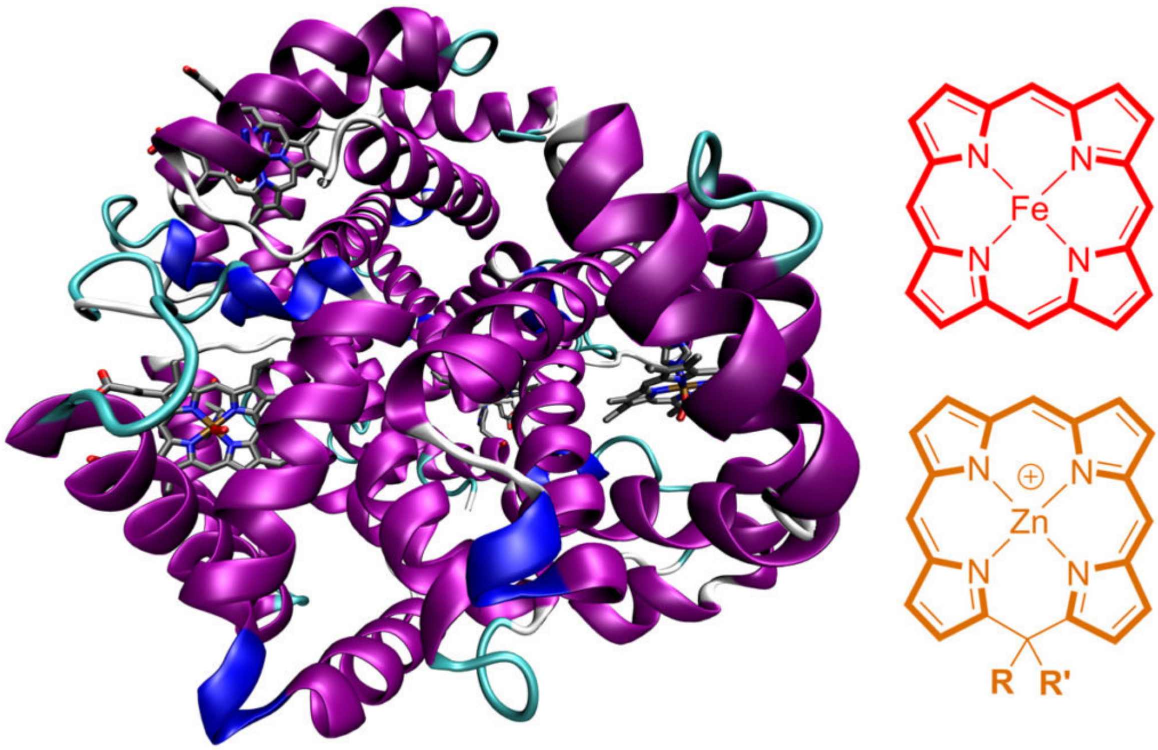

Fig. 2. Haemoglobin 3D structure (left; 1GZX, taken from PDB), and comparison of molecular porphyrin (red) and isoporphyrin (brown) structures (right).

Chemists provide help in this context by the synthesis of artificial dyes which show similar structures as the natural prototypes, but interact with light of a different and milder energy range. The human body shows an increased window of transparency for the high-energy end of the near-infrared light (NIR light), and it could be shown, that the section between wavelengths of about 800 – 950 nm offers advantages over using visible or UV light for PDT research, like much milder irradiation, and higher penetration depths.

A small variation of the porphyrin macrocycle of hemes leads to the *isoporphyrin* core. Since the 1960s it has been known from work initiated by the later Nobel laureate R. B. Woodward that such a variation provides the desired impact on the light absorption abilities of heme-related dyes (Fig. 2). However, the synthesis of such isoporphyrins proved quite difficult, and as other concepts leading to porphyrin-like NIR dyes are available, only little research was done in this field over the last 50 years.

We have now found a simple one-pot method which produces long-sought isoporphyrins in meaningful quantities. The finding was completely serendipitous, and it came off investigations to optimize the synthesis of yet another porphyrin analogue, the corrole. Beside the simplicity of this approach, many similar isoporphyrins carrying different peripheral groups as well as different metal centres are made generally accessible which highlights the great value of this finding. This simple one-pot procedure for isoporphyrin preparation now paves the way for further investigations on the isoporphyrins as possible NIR-dyes with use in PDT.

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