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Photodynamic Therapy and Photothermal Therapy using Porphyrins

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Perspective

Over the last decade, the field of nanomedicine has grown in popularity. Long circulation durations, high payload delivery, multimodal functionalization potential, and variable size are all advantages of organic nanoparticles for medicinal applications. Porphyrins offer a unique platform for the development of multifunctional imaging agents, hence integrating porphyrins into nanostructures has received a lot of attention. The PDT drug Visudyne® (manufactured by QLT Inc. of Vancouver, Canada), a lipid-based formulation encapsulating benzoporphyrin derivative monoacid ring A (BPD-MA), which is FDA authorised for age-related macular degeneration, is one of the most well-known instances of a porphyrin-carrying nanoparticle. Because of the lack of stability, solubility, and/or biological value as porphyrin content increases, the field has been unable to generate high-payload targeted porphyrin-based nanoparticles.

Porphyrin-lipid was titrated into a normal liposome composition to maximise the porphyrin concentration per nanoparticle and evaluate the influence of porphyrin-lipid on the characteristics of the nanovesicles. There were two key findings:

1. Nano vesicles could be made entirely of porphyrin-lipid subunits, allowing for a high payload delivery of porphyrins (80,000 porphyrins per porphysome nanovesicle), and

2. Increasing the porphyrin-lipid content within each nanovesicle resulted in greater fluorescence self-quenching. The optical energy absorbed after laser irradiation is efficiently converted into heat, generating temperatures comparable to inorganic nanoparticles such as gold nanorods, due to porphysomes' high optical extinction and extreme fluorescence self-quenching (109 cm^2 M1 at visible/near-infrared wavelengths).

Inorganic nanoparticles are appealing multifunctional agents for applications such as photothermal therapy and photoacoustic imaging because of their excellent biophotonic characteristics. Inorganic nanoparticles, on the other hand, are not biodegradable; therefore their long-term toxicity and *in vivo* clearance are frequently a source of worry. Porphysomes may be able to overcome these obstacles since they have significant biophotonic qualities and are made up entirely of organic porphyrin-lipid subunits that have been demonstrated to be nontoxic at high doses, enzymatically degradable, and biodegradable *in vivo*. Porphysomes are effective photothermal treatment agents. Porphysomes or saline were administered intravenously into KB xenograft-bearing mice, which were then laser irradiated. Mice given both porphysomes and laser irradiation had cancers totally eradicated, but mice given either laser alone or porphysomes alone (without laser irradiation) had tumours completely eradicated.

These biophotonic features can be used for more than only therapy and imaging. Photoacoustic imaging is a new method that detects ultrasonic vibrations created by a light-absorbing substance, allowing for high-resolution and contrast imaging deep within tissue. Porphysomes have photoacoustic characteristics that are structure-dependent. Porphysomes produce a significant photoacoustic signal while they are intact; however, when the nanoscale structure is disrupted, the photoacoustic signal is reduced. Sentinel lymph node mapping in rats demonstrated the ability of porphysomes to operate as photoacoustic contrast agents. The contrast supplied by porphysomes allowed the sentinel lymph node, secondary lymph vessels, and inflowing lymph vessels to be identified after injection.

The porphyrin fluorescence is restored once the nanostructure of porphysomes is disrupted, allowing porphysomes to be used for activatable fluorescence imaging. Porphysomes injected into a KB xenograft-bearing mouse's solid tumour showed a rise in fluorescence 48 hours later, showing that the porphysomes had reached, aggregated, and been taken up by tumour cells at the target region. In addition to restoring the porphyrin's fluorescence, uptake in cells and dissociation of the nanovesicles may also restore the porphyrin's phototoxicity, allowing porphysomes to be used for photodynamic treatment. Porphysomes also have liposome-like characteristics. Chemotherapy medications like doxorubicin might be actively loaded into porphysomes' vast aqueous core. Porphysome surfaces could potentially be easily functionalized. Porphysomes could be used to actively target tumours by adding lipids conjugated with biological surface indicators such as the folate receptor, which are overexpressed by cancer cells.

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