



Review

The novel polymeric systems for photodynamic therapy technique



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ABSTRACT

Photodynamic therapy (PDT) is a medical treatment in which a combination of a photosensitizing drug and visible light causes destruction of selected cells. Over the past two decades, photodynamic therapy has enjoyed a period of laboratory and in the clinic. Although still widely considered to be an experimental technique, its status and value within modern clinical practice continues to grow. The PDT field has, to date, been dominated by a small number of pharmaceutical companies inhabited almost exclusively by clinicians and those involved in fundamental scientific research. True pharmaceutical formulation development has been limited, to some extent, by financial constraints. If PDT is to realize its undoubted potential in clinical practice it is important that awareness of the need for appropriate photosensitizer delivery systems is raised. Accordingly, this article deals with the innovations pertaining to drug delivery systems for photodynamic therapy as disclosed in recent patent literature.

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1. Application of biodegradable polymeric nanoparticles in photodynamic technique

In vitro photocytotoxicity and cellular uptake of biodegradable polymeric nanoparticles loaded with photosensitizer mTHPP have been studied. As the first part of a continued research on conversion of N-sulfonato-N,O-carboxymethylchitosan (NOCCS) to useful biopolymer-based materials, large numbers of carboxylic functional groups were introduced onto NOCCS by grafting with polymethacrylic acid (PMAA). The free radical graft copolymerization was carried out at 70 °C, bis-acrylamide as a cross-linking agent and persulfate as an initiator. These results show that the nanoparticles have high loading capacity and stability. These

nanoparticles are suitable as carriers for photodynamic therapy in vivo [1]. Mohammad Reza Saboktakin et al. have been discussed some of the interesting findings and applications of modified chitosan (MCS) and their derivatives in different areas of drug delivery. This review highlights the important applications of MCS in the design of various novel delivery systems like liposomes, microspheres, microcapsules, and nanoparticles. In addition to their well-known effects on drug solubility and dissolution, bioavailability, safety, and stability, their uses as recipients in drug formulation are also discussed. This review also focuses on various factors influencing inclusion complex formation because an understanding of the same is necessary for proper handling of the seversatile materials. Some important considerations in selecting MCS in drug formulation such as their commercial availability, regulatory status, and patent status are also summarized [2]. Photodynamic therapy (PDT) is a medical treatment in which a combination of a photosensitizing drug and visible light causes

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destruction of selected cells. Over the past two decades, photodynamic therapy has enjoyed a period of intense investigation, both in the laboratory and in the clinic. Although still widely considered to be an experimental technique, its status and value within modern clinical practice continues to grow. The PDT field has, to date, been dominated by a small number of pharmaceutical companies and inhabited almost exclusively by clinicians and those involved in fundamental scientific research. True pharmaceutical formulation development has been limited, to some extent, by financial constraints. If PDT is to realize its undoubted potential in clinical practice it is important for appropriate photosensitizer delivery systems is raised. Accordingly, this article deals with the innovations pertaining to drug delivery systems for photodynamic therapy as disclosed in recent patent literature [3]. Nano delivery systems have shown considerable promise in increasing the solubility and delivery efficiency of hydrophobic photosensitizers for photodynamic therapy (PDT) applications. In this study, has been reported the preparation and characterization of polymeric micelles that incorporate protoporphyrin IX (PpIX), a potent photosensitizer, using non-covalent encapsulation and covalent conjugation methods. Depending on the incorporation method and PpIX loading percentage, PpIX existed as a monomer, dimer or aggregate in the micelle core. The PpIX state directly affected the fluorescence intensity and $^1\text{O}_2$ generation efficiency of the resulting micelles in aqueous solution. Micelles with lower PpIX loading density (e.g. 0.2%) showed brighter fluorescence and higher $^1\text{O}_2$ yield than those with higher PpIX loading density (e.g. 4%) in solution. However, PDT efficacy in H2009 lung cancer cells showed an opposite trend. In particular, 4% PpIX-conjugated micelles demonstrated the largest PDT therapeutic window, as indicated by the highest phototoxicity and relatively low dark toxicity. Results from this study contribute to the fundamental understanding of nanoscopic structure–property relationships of micelle-delivered PpIX and establish a viable micelle formulation (i.e. 4% PpIX-conjugated micelles) for in vivo evaluation of antitumor efficacy [4]. Given the ever increasing problem of antibiotic resistance in nosocomial pathogens it is important to promote alternate technologies that may be more effective than current antibiotics. This article reviews photodynamic antimicrobial chemotherapy (PACT), a technology based on the use of a photosensitizer activated by visible light illumination and found to be effective against most types of microbial pathogens, including those resistant to antibiotics. PACT nonetheless has certain limitations, particularly against internal and blood-borne infections. To this end, we are developing chemiluminescent photodynamic antimicrobial therapy (CPAT). This review also summarizes our recent data on CPAT. The practical advantages of CPAT emphasize that this novel technique could expand efforts to control nosocomial pathogens, including those responsible for systemic infections [5] (Fig. 1).

Photodynamic therapy (PDT) is an emerging theranostic modality for various cancer as well as non-cancer diseases. Its efficiency is mainly based on a selective accumulation of PDT and imaging agents in tumor tissue. The vascular effect is widely accepted to play a major role in tumor eradication by PDT. To promote this vascular effect, we previously demonstrated the interest of using an active-targeting strategy targeting neuropilin-1 (NRP-1), mainly over-expressed by tumor angiogenic vessels. For an integrated vascular-targeted PDT with magnetic resonance imaging (MRI) of cancer, we developed multifunctional gadolinium-based nanoparticles consisting of a surface-localized tumor vasculature targeting NRP-1 peptide and polysiloxane nanoparticles with gadolinium chelated by DOTA derivatives on the surface and a chlorin as photosensitizer. The nanoparticles were surface-functionalized with hydrophilic DOTA chelates and also used as a scaffold for the targeting peptide grafting. In vitro investigations demonstrated the

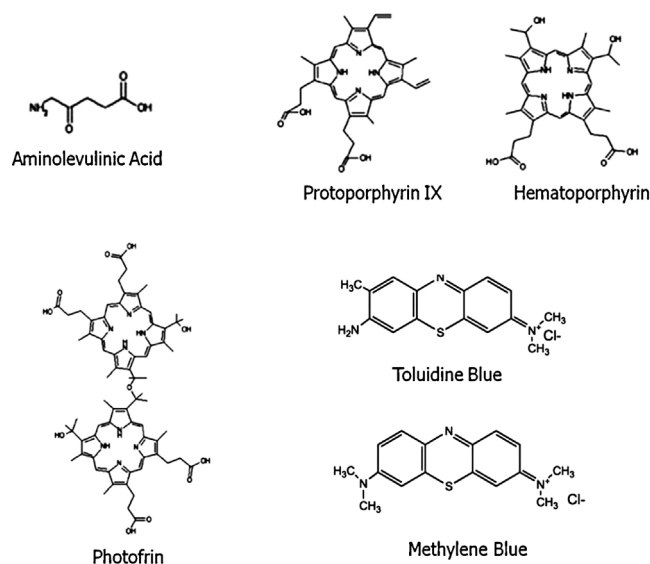


Fig. 1. Chemical structures of some photosensitizers used in PDT. Aminolevulinic acid, hematoporphyrin and photofrin are approved for clinical use.

ability of multifunctional nanoparticles to preserve the photophysical properties of the encapsulated photosensitizer and to confer photosensitivity to MDA-MB-231 cancer cells related to photosensitizer concentration and light dose. Using binding test, we revealed the ability of peptide-functionalized nanoparticles to target NRP-1 recombinant protein. Importantly, after intravenous injection of the multifunctional nanoparticles in rats bearing intracranial U87 glioblastoma, a positive MRI contrast enhancement was specifically observed in tumor tissue. Real-time MRI analysis revealed the ability of the targeting peptide to confer specific intratumoral retention of the multifunctional nanoparticles [6]. In this research has been addressed a highly interdisciplinary field, the use of nanomaterials as carriers for singlet oxygen photosensitizers and their potential applications in photodynamic therapy. In particular, recent advances in the use of nanoparticles including inorganic oxide-, metallic-, and polymer-based nanocomposites as photo sensitizer carriers are highlighted. The advantages and shortcomings of these diverse have been approached as far as their application for photodynamic therapy is concerned. Fullerenes and their derivatives are also included, focusing on recent studies on their structure, properties, and ability to generate singlet oxygen [7]. The photodynamic therapy (PDT) is a promising treatment modality for cancer. PDT is based on the concept that photosensitizers, when exposed to light of specific wavelength, generate cytotoxic reactive oxygen species (ROS) capable of killing tumor cells. The effectiveness of PDT has been limited in part by the lack of photosensitizers that accumulate sufficiently in tumor cells and poor yield of ROS from existing photosensitizers. In this report has been investigated whether aerosol OT-alginate nanoparticles can be used as a carrier to enhance the therapeutic efficacy of a model photosensitizer, methylene blue. Methylene blue loaded nanoparticles were evaluated for PDT effectiveness in two cancer cell lines, MCF-7 and 4T1. Encapsulation of methylene blue in nanoparticles significantly enhanced intracellular ROS production, and the overall cytotoxicity following PDT. It also resulted in higher incidence of necrosis. Greater effectiveness of nanoparticles could be correlated with higher yield of ROS with nanoparticle-encapsulated methylene blue. Further, treatment of tumor cells with nanoparticle-encapsulated methylene blue resulted in significant nuclear localization of methylene blue while free drug treatment resulted in its accumulation mainly in the endolysosomal vesicles. In conclusion, encapsulation of methylene blue in aerosol OT-alginate nanoparticles enhanced its anticancer

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