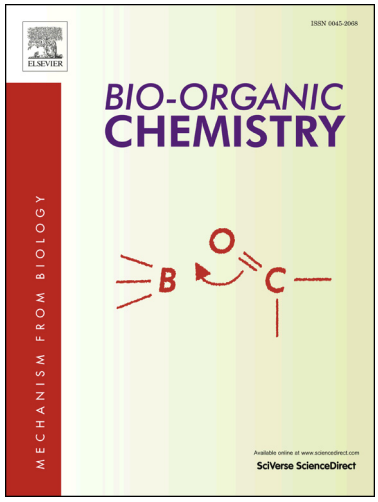

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Synthesis of 2-morpholinetetraphenylporphyrins and their photodynamic activities

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Abstract: A series of 2-morpholinetetraphenylporphyrins functionalized with various substituents (Cl, Me, MeO group) at 4-phenyl position were prepared via nucleophilic substitution of 2-nitroporphyrin copper derivatives with morpholine by refluxing under a nitrogen atmosphere and then demetalization. Their basic photophysical properties, intracellular localization, cytotoxicities *in vitro* and *in vivo* were also investigated. All synthesized photosensitizers exihibited longer maxima absorption wavelengths than Hematoporphyrin monomethyl ether **(HMME)**. They showed low dark cytotoxicity compared with that of **HMME** and were more phototoxic than **HMME** against Eca-109 cells *in vitro*. **M3** also exhibited better photodynamic antitumor efficacy on BALB/c nude mice at a lower concentration. Therefore, **M3** is a promising antitumor photosensitizer in photodynamic therapy application.

Keywords: photosensitizer, photodynamic therapy, porphyrin, antitumor

1. Introduction

Photodynamic therapy (PDT) is a clinically approved, minimally invasive protocol for treatment and is an attractive therapeutic procedure utilizing a photosensitizer (PS) activated by light of appropriate wavelength (phototherapeutic window 600 − 850 nm) to generate highly reactive oxygen species (ROS)[1-4]. ROS are chemically reactive radicals or non-radical molecules derived from molecular oxygen and include singlet oxygen, peroxide, superoxide and the hydroxyl radical[5, 6]. The ROS mediated mechanism is the major cause underlying the efficacy of PDT[7]. ROS mainly initiates three biological mechanisms that make PDT an effective anticancer procedure: (1) direct tumor killing induced by the ROS; (2) tumor-associated vascular shutdown and massive ischemic death; (3) activation of antitumor immune memory and systemic response[8]. Compared with traditional cancer therapies such as surgery and chemotherapy, PDT has the advantage of dual selectivity in that the PS can be targeted to its destination cell or tissue without destructing the surrounding normal tissues[9].

Over the past decade, a substantial effort has been put into the development of various classes of PS, the synthesis of PS with desired physical, chemical and biological properties is considered to be an