

Experimental Animal Models for Preclinical Evaluation of Symmetrical Diiodinated Squaraine Dye

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DESCRIPTION

Photodynamic Therapy (PDT) is emerging as a promising noninvasive treatment for cancers. It involves three key components; a photosensitizer, light and tissue oxygen. Photodynamic therapy involves administration of a tumor localizing photosensitizing agent, followed by the activation of the agent by light of a specific wavelength. This therapy results in a sequence of photochemical and photo biological processes that cause irreversible photo damage to tumor tissue. Photodynamic Therapy (PDT) has emerged as an alternative strategy for treating cancer. PDT consists of three main components: a photosensitizer, light, and oxygen. PDT takes advantage of an appropriate wavelength of light that excites a photosensitizer to a triplet energy state. In the presence of molecular oxygen, energy is transferred to relax the excited state of the photosensitizer. This energy transfer in turn excites molecular oxygen to form excited, singlet state oxygen. Singlet oxygen induces cell death via damaging oxidation or redox-sensitive cellular signaling pathways, thus mediating the effects of PDT. Intriguingly, PDT has also been shown to regulate processes beyond tumor cell death including tumor angiogenesis and modulation of the immune system. Each photosensitizer is activated by light of a specific wavelength. This wavelength determines how far the light can travel into the body. An ideal photosensitizer should meet some of the following criteria that are clinically relevant: a commercially available pure chemical, low dark toxicity but strong photocytotoxicity, good selectivity towards target cells, long-wavelength absorbing, rapid removal from the body and ease of administration through various routes. These criteria

provide a general guideline for comparison. Although some photosensitizers satisfy all of or some of these criteria, there are currently only a few photosensitizers that have received official approval around the world. However, PDT with the currently FDA-approved photosensitizers is not without adverse effects. For example, Photofrin, the first systemic drug to be approved, is well known for causing an intense inflammatory and necrotic reaction at the treated site and prolonged widespread photosensitivity for up to several weeks post-PDT, thereby imposing severe limitations on the lifestyle. Because of this and other drawbacks of Photofrin, many additional photosensitizers have been synthesized, and a few of them have developed into FDA-approved drugs or are in clinical trials. Interest in the synthesis and evaluation of new photosensitizers for use in PDT has grown as a result of both the encouraging initial clinical results of this therapy and the documented need to improve upon the limitations of currently available photosensitizers. The dye selected in our study- Symmetric diiodinated squaraine- is one of the newly developed photosensitizers. We have done the in vivo biodistribution of the dye on normal and skin tumor induced animal models to check the retention time of the dye. Before analyzing the therapeutic efficacy of the compound as a photosensitizer, it should be confirmed that it does not elicit any toxic manifestations in the body, when not illuminated. One among the most important criteria of an ideal photosensitizer is that it should induce no dark-toxicity; i.e., it should be non-toxic in the dark. Thus we have checked whether symmetrical diiodinated squaraine is an ideal photosensitizer in this aspect by checking the antioxidant status of dye administered mice.

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Received: June 07, 2021; **Accepted:** June 21, 2021; **Published:** June 28, 2021

Citation: Saki T (2021) Experimental Animal Models for Preclinical Evaluation of Symmetrical Diiodinated Squaraine Dye. *Biochem Anal Biochem.* 10:e175.

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