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# Fullerene ($C_{60}$) Evaluation for Photodynamic Therapy

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## Extended Abstract

Cancer is the second leading cause of death globally [1]. World Health Organization reported 9.6 million cancer-related deaths only in 2018 [2]. Although there have been advances in cancer therapy, the development of anti-tumor strategies faces many limitations. The main cancer-treating methods—chemotherapy and radiotherapy—compromise the host's immune system and have many other systemic side effects [3]. Recently, photodynamic therapy (PDT) has attracted attention in cancer treatment due to its non-invasive and highly selective properties [4], [5]. The idea behind PDT is using a photosensitizer with varying affinity to malignant and normal cells resulting in different concentrations of the agent in cells. Subsequently, an appropriate wavelength light irradiation on target cells produces reactive oxygen species (ROS) due to the photosensitizer leading to cellular damage [6].

Various photosensitizers are used in PDT. Most of them are porphyrin-based dyes with low quantum yield, little tumor targetability, high-power laser light exposure requirement, and general side effects on healthy tissue [7]. Meantime, fullerene ($C_{60}$), a new class of nanocarbon molecules with 60 carbon atoms in a closed cage structure, has been introduced as an efficient and non-toxic photosensitizer [8]. Due to the unique photoproduction abilities of $C_{60}$ fullerenes, they can generate singlet oxygen and other ROS ($O_2^-$, $H_2O_2$, $HO^\bullet$) under the influence of visible light irradiation [9]. Besides, $C_{60}$ accumulates in malignant cells selectively and inhibits key enzyme systems competitively [10]. This reduces systematic side effects in the body compared to chemotherapy and other photodynamic agents [11]. However, $C_{60}$ fullerenes have some limitations. For example, $C_{60}$ is insoluble in polar solvents, which limits its application in biological studies. Therefore, $C_{60}$ bioavailability must be enhanced by adding water-soluble functional groups [12], [13]. This study reviewed related studies since 1996 about different hydrophilic agents, such as polyethylene glycol (PEG), nano-silica, carboxylic acids, human serum albumin, glycogen, polyethylene oxide, glycol chitosan, and viral nanoparticles, added to $C_{60}$ to increase water solubility. We analyzed the reported results for $C_{60}$ hydrophilic agent combinations that were examined in vivo or in vitro under a specific wavelength light irradiation. As a result of the cytotoxicity ability of the $C_{60}$-agent combination, cell viability was used as one of our main indicators to compare PDT efficacy of various $C_{60}$-agent combinations. It was found that $C_{60}$ conjunctions could increase the functionality of fullerenes in treating different cancer cells.

PDT efficacy is not all, and we need to focus on the side effects as well. The major challenge in cancer treatment strategies is to limit systemic side effects. For this purpose, drug delivery systems (DDSs) have been designed to destroy target cells selectively. They also control and prolong drug release by protecting the drug from degrading enzymes [14]. A DDS consists of three main parts: 1) an addressing unit to recognize selected targets, 2) a multiplying unit to increase the number of drug molecules, and 3) an active biological unit. In the second part of our review article, we explained different substances like liposome, graphene, transferrin, pullulan, etc. as drug delivery agents added to $C_{60}$ to maximize its therapeutic effects and minimize its side effects spontaneously [15]. In conclusion, drug delivery systems using $C_{60}$ showed a strong anti-tumor efficacy compared to free drugs under irradiation.

In the last part of this study, we investigated the application of porphyrin-$C_{60}$ and chlorine-$C_{60}$ dyads in PDT to enhance ROS production in PDT. Recently, porphyrins, phthalocyanines, and chlorines have been recommended as therapeutic properties in PDT. Based on recent studies, we evaluated the functionality of porphyrin-$C_{60}$ and chlorine-$C_{60}$ dyads for producing long-lived radical ion pairs under irradiation, which makes these combinations very efficient sensitizers for PDT [16]. Finally, the combination could reduce cell viability significantly under light irradiation.

In this study, for the first time, we explored the capability of $C_{60}$ fullerenes as effective photosensitizers and revealed their cons and prose for treating cancer diseases. Results will be useable for a broad audience, from engineers to medical researchers, to chemically modify fullerene and apply it as a cancer treatment photodynamic agent.

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