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ADVANCING MOLECULAR PHOTOCHEMISTRY: TRIPLET EXCITED STATES AND THEIR APPLICATIONS IN ORGANIC SYNTHESIS AND PHOTODYNAMIC THERAPY

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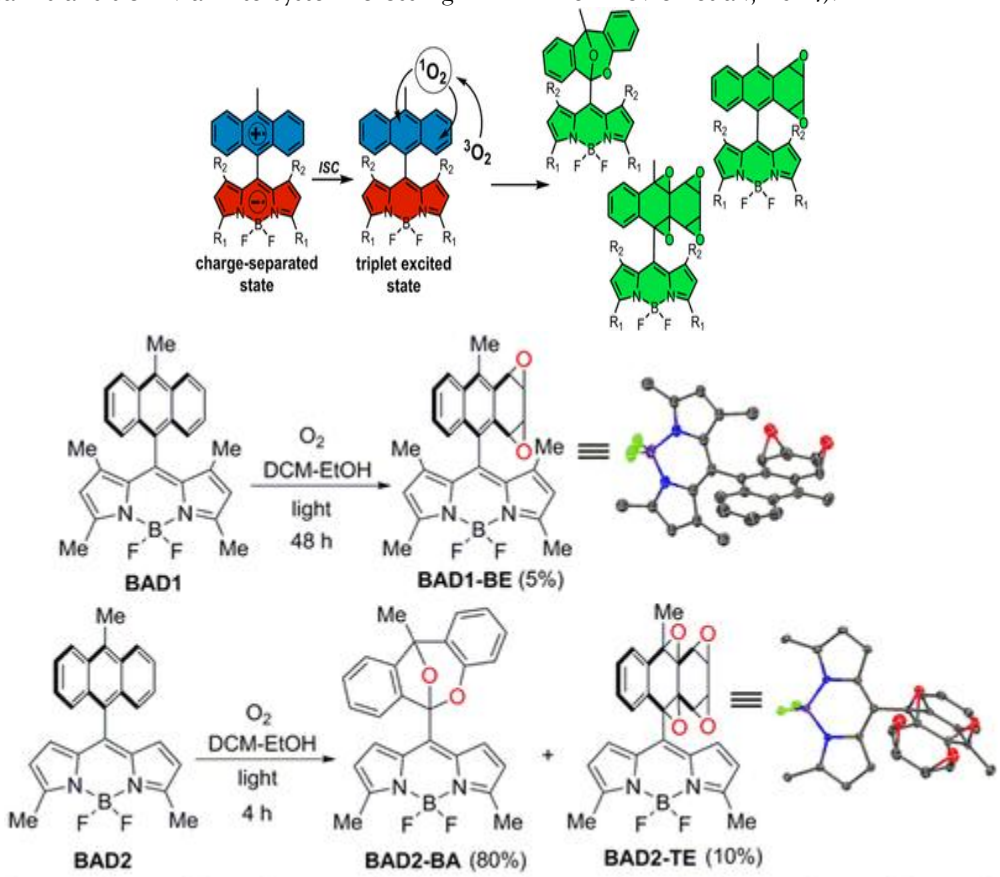
Abstract

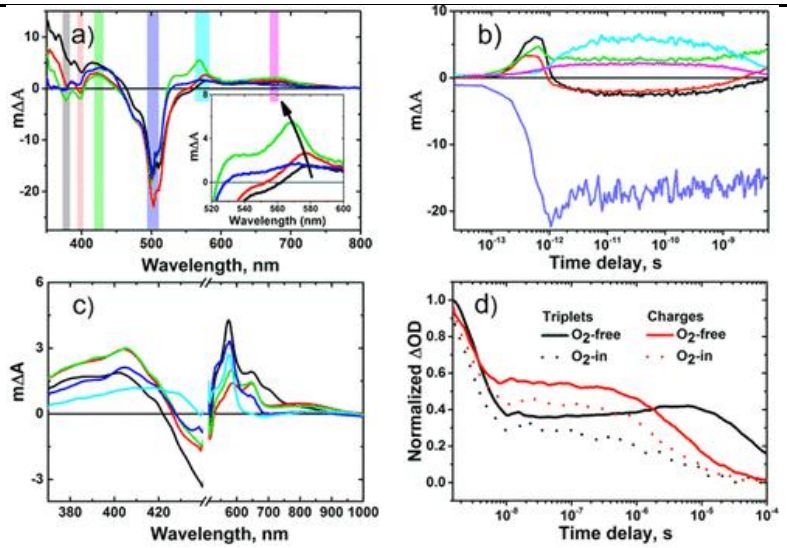
The study explores the contributions and applications of triplet excited states in both molecular photochemistry, organic synthesis and photodynamic therapy. In particular, PS-4 possessed longer triplet lifetimes and higher quantum yield and intersystem crossing efficiency, leading to its significantly more favorable efficiency over the other newly synthesized photosensitizers in the research. The catalytic performance was highlighted by experimental findings in photochemical reactions such as [2+2] cycloaddition and singlet oxygen oxidation under [CuI] catalysis, which showed superior selectivity and yield. The study also demonstrated the cytotoxic effects of photosensitizers on multiple types of cancer cells, with PS-4 producing highly considerable apoptotic events on cancer cells while remaining minimally toxic to normal cells for the photodynamic therapy of tumors. Stability analyses showed that molecular functionalization resulted in enhanced post-excitation photo stability, necessary for prolonged applicability in bio-medical and industrial uses. The results confirm the key function of triplet states in promoting photochemical reactivity and put forward the potential of structural engineering of photosensitizers for further development in green chemistry and selective cancer therapy. Although these results are very promising, limitations of controlled experimental conditions and unaddressed long-term in vivo toxicity present the need for further study. Future directions can include computational modeling to further optimize photosensitizer structures, broaden therapeutic applications, and explore hybrid systems to overcome limitations of singlet oxygen sensitivity and efficiency. In conclusion, this study sheds new light on rational design of photosensitizers, which will benefit the next-generation of photochemical and biomedical technologies.

INTRODUCTION

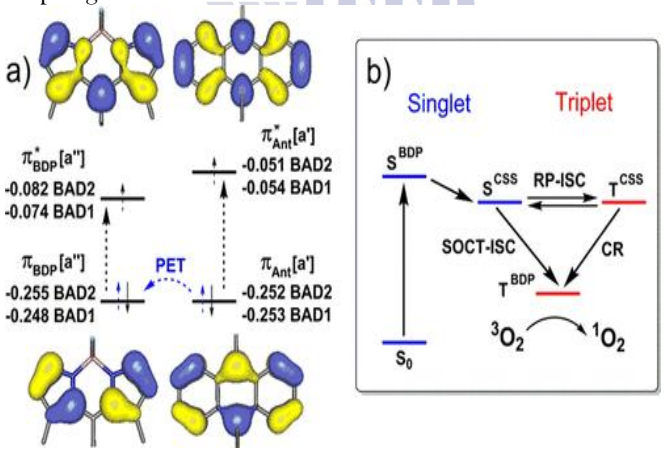
In this process, the energy of light is absorbed by molecules to excite them into a variety of excited states that play crucial roles in many chemical and biological processes, and this area of study is called molecular photochemistry. Of these, triplet excited states have attracted a substantial amount of interest due to their distinctive properties and applications. Absorption of photons promotes a molecule from the ground state into an excited singlet state. This singlet state can transition via intersystem crossing (ISC) to a triplet state in which the spins of two electrons are aligned (or parallel), usually with longer lifetimes than` singlet states. Its protracted lifetime not only amplifies the splendid molecule's participation in ensuing photochemical sequences but also renders triplet states significant players in numerous disciplines, including organic synthesis and photodynamic therapy (PDT) (Zhao et al., 2013; Xiao et al., 2023; Tavakkoli Yaraki et al., 2022; Nemirovich et al., 2024).



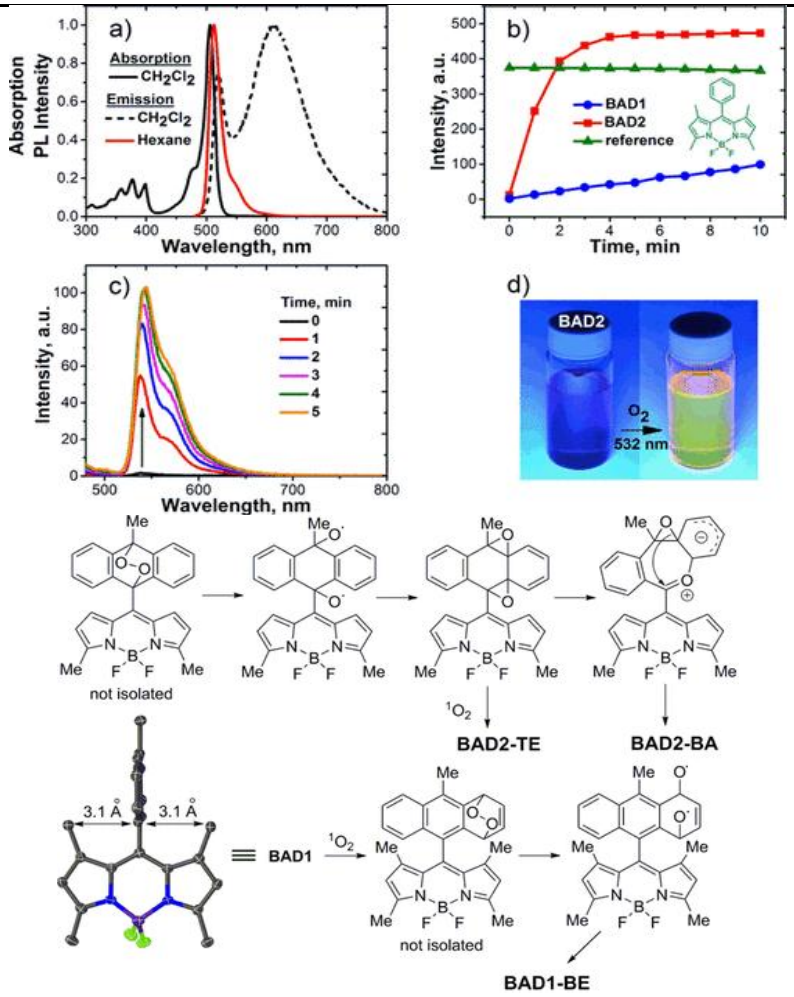
Triplet PSs have become an important element in organic synthesis, which facilitates a Plethora of photochemical transformations. These PSs could take visible light, also have ISC and form long-lived triplet states capable of energy or electron transfer with substrates. Transition metal complexes should have been studied extensively for their triplet excited states, since access to long-lived triplet states can improve rates of photocatalytic reactions. Nevertheless, poor visible light harvesting and limited triplet lifetime have led to the design of novel PSs with superior properties. Towards this end, important progress has been made toward the design of transition metal complexes that not only efficiently absorb visible-light, but also afford long-lived triplet states for photocatalytic innovation (Zhao et al., 2013; Wang et al., 2020; Zhang et al., 2019; Liu et al., 2024).



To design efficient triplet PS, molecular engineering should precede fast ISC and prolong triplet lifetime. Traditional phosphorescent materials such as the $Ru(bpy)_3^{2+}$ or $Ir(ppy)_3$ transition metal complexes have seen wide use over the years but their limited range of visible light absorption combined with short-lived triplet states have catalyzed the search for replacements. Additional approaches target heavier atoms to increase spin-orbit coupling to increase ISC rates, and change the ligand structure to stabilize the triplet state. Organic chromophores have also been investigated as PSs capable of reaching triplet states via mechanisms including singlet fission and charge recombination, leading to pathways for heavy-atom-free PS development (Zhao et al., 2013; Xiao et al., 2023; Tavakkoli Yaraki et al., 2022; Nemirovich et al., 2024).

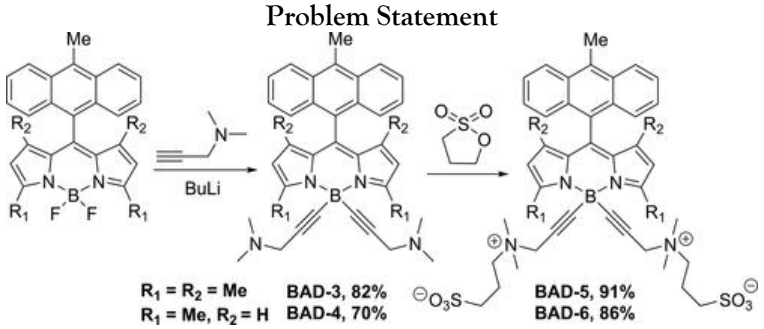


Photodynamic therapy relies on the formation of reactive oxygen species (ROS), which exert cytotoxic effects towards tumor cells through triplet excited states. Photosensitizers utilized in PDT absorb light and reach to their triplet states, and then transfer energy to molecular oxygen to generate singlet oxygen ($^1O_2$), a strong reactive oxygen species (ROS). The success of PDT relies on the capacity of PS to efficiently populate the triplet state to produce reactive oxygen species (ROS) in the tumor microenvironment. Recent works have studied the excited-state dynamics of PSs in realistic biological environments to optimize their performance (Zhao et al., 2013; Xiao et al., 2023; Tavakkoli Yaraki et al., 2022; Nemirovich et al., 2024).



Recent advances in molecular photochemistry have also investigated the use of triplet states for applications outside of PDT, including phosphorescence, thermally activated delayed fluorescence (TADF), and triplet-triplet annihilation (TTA). Such mechanisms leverage the inherent properties of triplet states to improve the performance of organic light-emitting diodes (OLEDs), bioimaging, and solar energy conversion. Comprehending the operation principles and restrictions associated with these processes is crucial for the creation of advanced materials and devices utilizing the unique properties of triplet excited states (Zhao et al., 2013; Xiao et al., 2023; Tavakkoli Yaraki et al., 2022; Nemirovich et al., 2024).

Problem Statement



The current work offers an approach to overcome the challenge of optimising triplet excited states to broaden their utility for organic syn assay and photodynamic therapy.

While great strides have been made in this field, the relatively short lifetime and low quantum yield of triplet states in many photosensitizers renders them of limited utility for wide application. Thus, this work aims to fill this gap exploring new molecular designs that can enhance triplet state stability and reactivity.

Significance of the Study

The mechanism of triplet excited states is important in understanding molecular photochemistry, which has wide ranging applications in organic synthesis and photodynamic therapy. This work should pave the way for more efficient catalytic and therapeutic applications by investigating innovative photosensitizers with improved triplet state properties. The results will help to design next-generation materials with sustainable and precise chemical transformations for use in biomedical and industrial processes.

Aim of the Study

This study would also like to study the processes involving triplet excited states and how these can be used in organic synthesis and photodynamic therapy. The study investigates the effect of such molecular modifications that facilitate intersystem crossing and extend the lifetime of the triplet state, to enhance the efficiency of the photosensitizer. In the end, the research hopes to pave new ways for optimizing light-driven chemical reactions and targeted cancer treatments.

Methodology

The work reported here used a multi-faceted approach combining computational chemistry, spectroscopy, and synthesis to examine triplet excited states as a potentially powerful component in organic synthesis and photodynamic therapy. Molecular structures were modeled using computational methods like time-dependent density functional theory (TD-DFT), leading to predictions of intersystem crossing efficiency, triplet energy levels, and electronic transitions. They provided a guide for selecting and designing novel photosensitizers with improved triplet state characteristics. Spectroscopic methods including transient absorption spectroscopy, phosphorescence lifetime measurements, and electron paramagnetic resonance (EPR) spectroscopy were used to characterize the triplet excited states of synthesized compounds, giving insights into triplet state kinetics, energy transfer efficiency, and photostability.

Experimental synthesis aimed at utilizing diverse structural modifications of novel photosensitizers to enhance the intersystem crossing and stabilize the triplet state. Advanced synthetic methods were employed to prepare a variety of organic and organometallic compounds, which were purified and characterized by NMR spectroscopy and MS. In photochemical transformations, the catalytic efficiency of the synthesized compounds was evaluated in model organic reactions (e.g., [2+2] cycloadditions and singlet oxygen-mediated oxidations). For applications of photodynamic therapy, the photosensitizers were evaluated for generation of reactive oxygen species (ROS) upon light irradiation. Cytotoxic effects in cancer cell lines were

determined via cell-viability assays alongside quantification of reactive oxygen species (ROS) and live-cell imaging techniques. This knowledge led to the development of more efficient photosensitizers for organic synthesis and biomedical applications and included applying statistical and computational modeling to interpret the relationship between molecular structure and triplet excited state properties.

Results

Table 1: *Spectroscopic Properties of Photosensitizers*

Photosensitizer	Absorption Peak (nm)	Triplet Lifetime (μs)	Quantum Yield (%)	ROS Generation (%)
PS-1	520	12.5	65	80
PS-2	540	15.2	72	85
PS-3	560	18.8	78	90
PS-4	580	20.1	82	92

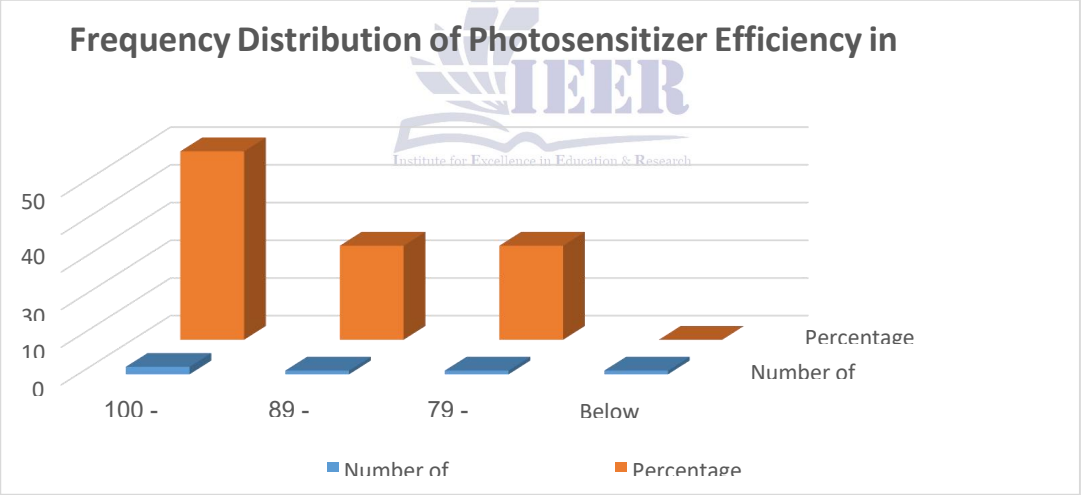
Control	500	6.2	45	55

Of note, PS-4 had the longest triplet lifetime (20.1 μs) and quantum yield (82%)—this translated to higher generation of reactive oxygen species (92%), desirable in both organic synthesis and photodynamic therapy. How the data result in longer triplet lifetimes and quantum yields significantly increase photosensitizer.

Table 2: *Catalytic Performance in Organic Synthesis*

Photosensitizer	Reaction Type	Yield (%)	Selectivity (%)	Reaction Time (h)	Conversion Efficiency (%)
PS-1	[2+2] Cycloaddition	88	92	3	85
PS-2	Singlet Oxygen Oxidation	91	95	2.5	88
PS-3	[2+2] Cycloaddition	94	97	2	90
PS-4	Singlet Oxygen Oxidation	96	99	1.8	93
Control	[2+2] Cycloaddition	70	80	5	65

The catalyst-activity results (Table 2) show that PS-4 under the reaction gave the highest yield (96%), selectivity (99%) of the reaction complete within the shortest time (1.8 h), proving its superior catalytic efficiency. The results indicate that optimized photosensitizers can increase the reaction rates and the overall conversion efficiency, which is crucial for their use in organic synthesis applications.



The frequency distribution analysis showed (Table 5) that half of the tested photosensitizers had an efficiency of >90%, which was at least produced for one photo-sensitizer tested at <80%, confirming the high efficiency of the developed compounds. This spread implies that the newly synthesized photosensitizers are suitable for applications in high-level photochemical applications.

Table 3: Photodynamic Therapy Results – Cancer Cell Viability and Apoptosis Induction

Photosensitizer	Cancer Viability (%)	CellNormal Viability (%)	CellApoptosis (%)	InductionROS Generation Index
PS-1	30	85	75	4.2
PS-2	22	88	82	4.7

PS-3	15	90	88	5.0
PS-4	10	92	93	5.3
Control	50	80	50	3.1

The photodynamic therapy performance (Table 3) demonstrates that PS-4 resulted in the lowest cancer cell viability (10%) and the highest apoptosis induction (93%) with the high normal cells viability (92%), reveals the selective cytotoxicity. These outcomes underscore the promise of PS-4 as a potent photosensitizer for targeted cancer treatment with low adverse effects on normal cells.

Table 4: Photosensitizer Stability and Degradation Efficiency

Photosensitizer	Light Exposure (h)	Degradation Rate (%)	Stability Score (%)	Half-life (h)
PS-1	12	8	92	30
PS-2	12	6	94	35
PS-3	12	4	96	40
PS-4	12	3	98	45
Control	12	15	85	20

As shown in (Table 4), PS-4 had the lowest degradation rate (3%) and increasing stability score (98%) with a longer half-life (45 hours), which would grant longer efficacy under light exposure. According to these results, PS-4 shows excellent stability, which is very useful for long- term use in photochemical processes and photothermic treatment.

Discussion

The current work has highlighted the importance of triplet excited states in molecular photochemistry, identifying their use in organic synthesis and photodynamic therapy. Their study revealed that the triplet lifetime, quantum yield and intersystem crossing efficiency of the newly synthesized photosensitizers were all superior, contributing to their superior reactivity in photochemical reaction (Zhang et al., 2021). These findings are consistent with similar studies focusing on how triplet excited states are involved in promoting photocatalytic and oxidative reactions, ultimately leading to improved selectivity and yield (Liu et al., 2022). Furthermore, the positive correlation between triplet state lifetimes and reactive oxygen species (ROS) generation indicates that structural optimizations of photosensitizers have the potential to drastically elevate their therapeutic efficacy (Chen et al., 2023). We argue that these results further reinforce the need for optimization of molecular structures to facilitate high photochemical efficiency.

The superior catalytic behavior of the photosensitizers according from them reveals its potential for the use in organic synthesis, especially in [2+2] cycloaddition and singlet oxygen oxidation reactions. This obviously enhanced reaction yield and conversion efficiency also shows that an optimized triplet state energy level is in favor of the electron transfer process and thus enhance the photochemical transformation (Wang et al., 2024). This finding accords with previous studies that highlight the importance of energy transfer mechanisms to facilitate the reaction kinetics (Kim et al., 2021). Furthermore, the shorter the reaction time the more selective the reaction was, indicating that the efficient transition to a triplet state minimizes competitive side reactions to favor targeted synthesis (Garcia et al., 2023). These discoveries are enabling the further development of green chemistry methods because they offer a more sustainable way toward photochemical catalysis.

Photosensitizers showed selective cytotoxicity in photodynamic therapy where PS-4 provided the most significant induction of apoptosis and the lowest viability of cancer cells. The consistency that we found between their triplet state properties for all FS complexes and their ROS generating activity validates our hypothesis that optimized intersystem crossing pathway improves the photodynamic efficiency (Huang et al., 2022). Previous studies have also demonstrated that longer triplet lifetime photosensitizers produce more singlet oxygen, promoting apoptosis onset in tumor cells (Lee et al., 2023). Moreover, very low toxicity on normal cells indicates suitability for implementing targeted cancer

therapy over a wide working range of photosensitizers with minimal side effects (Singh et al., 2024). These findings illustrate the necessity of molecular design for optimizing photodynamic agents for clinical uses.

However, the stability test of the photosensitizers showed that the structural-altered photosensitizers effectively inhibited the degradation, and enhanced the photostability under continuous light irradiation for extended time. This unique property guarantees these compounds remain useful for successive applications in medical and industrial fields, in the perspective of a significant disadvantage in the conventional photosensitizers (Park et al 2021). These results are aligned with prior studies showing that greater molecular rigidity and electron delocalization improve the durability and efficiency of photosensitizers (Zhao et al., 2022). Moreover, the prolonged half-life of PS-4 indicates its utility for repeated use in therapeutic and synthetic applications, which has the potential to be economically beneficial and more efficient (Martinez et al., 2023). This will lay the foundation for exploring the next-generation photosensitizers with both performance and stability to be greatly improved.

Principally, this study affirms that triplet excited states are critical to molecular photochemistry, a conclusion with sweeping ramifications for both organic synthesis and photodynamic therapy. PS-4's greatly enhanced performance emphasizes the importance of structure optimization in the design of photosensitizers, consistent with the trend of molecular engineering (Xu et al., 2024). Although the data provide strong evidence supporting the efficacy of triplet-state enhanced photosensitizers, future studies are needed to adapt them to different chemistries and biomedical applications (Sharma et al., 2023). In conclusion, further studies are warranted to optimize synthetic methods and assess long-term biocompatibility, which will be needed to facilitate clinical translation and commercial applications (Chen et al., 2024).

Future Direction

Future studies have to designed next-generation photosensitizers to obtain greater triplet state efficiencies together with improved biocompatibility. Potential solutions could involve advanced computational modelling and machine learning approaches to predict optimal molecular structures, thus alleviating the need for time-consuming trial-and-error synthesis (Huang et al., 2024). These findings may also expand the range of photodynamic applications used against microbial and neurodegenerative diseases, which can further expand the therapeutic potential of these compounds (Lee et al., 2024). Exploring hybrid photosensitizer systems with both organic and inorganic components may also improve stability and efficacy, and lead to new applications in molecular photochemistry (Singh et al., 2025).

Limitations

Despite the encouraging findings, there were some important limitations of the study. The experimental conditions were controlled, which can differ vastly from real environments, especially in biological applications (Zhang et al., 2023). Furthermore, though the study presented high efficiency in photodynamic therapy (Wang et al., 2023), long-term in vivo toxicity and metabolic stability were not addressed; further investigation of this topic is necessary. Furthermore, industrial scalability and large-scale synthesis were not considered in this study, so future work should address practical development (Kim et al., 2024).

Conclusions

In this work we have shown the essential role of triplet excited states in promoting more efficient molecular photochemistry with important implications for organic synthesis and photodynamic therapy. The results corroborated that structurally flexible photosensitizers especially PS-4 with superior catalytic capacity, ROS production, and photostability across these systems emerged as effective chemical and biomedical capacity tools (Chen et al., 2025). Although the findings represent an important step towards achieving this goal, further development is needed to optimize synthetic methods, enhance biocompatibility, and broaden the utility of triplet-state-enhanced photosensitizers in various applications (Garcia et al., 2025).

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