حساب TD-DFT لمادة BODIPY والمواد المرتبطة به كمتحسس ضوئي في المعالجة الديناميكية الضوئية

بثينه كامل* **أ. د. م وسام بشير**** **أ. د.م مصطفى صائم الدهر*****

الملخص

تم إجراء دراسة تظرية لمادة الـBodipy كمتحسس ضوئي في المعالجة الديناميكية الضوئية لخمس جزيئات حيث تم الاستبدال في الموقع 6 في كرموفورالـ Bodipy بعناصرمن العمود الخامس من الجدول الدوري مثل(N-P-As-Bi).تم الاعتماد على نظرية التابعية للكثافة (DFT) ونظرية التابعية للكثافة التابعة للزمن(TD-DFT) لحساب طاقة السوية الأرضية وطاقة السوية المثارة الأحادية والثلاثية وفروق الطاقة ($\Delta E_{S_1-T_1}$, $\Delta E_{T_1-S_0}$) .

وأطياف الإمتصاص الإلكترونية والإنتقال لعزم ثنائي القطب($S_0 \rightarrow S_n$) وغيرها من الخواص.

---

*طالبة دكتوراه، قسم الفيزياء، كلية العلوم، جامعة دمشق.

** المعهد العالي لبحوث الليزر وتطبيقاته، جامعة دمشق، سورية.

*** مخبر الفوتونات الطبية الحيوية ،قسم فيزياء وتقانة الليزر.

الكلمات المفتاحية: مادةالـ Bodipy، متحسس ضوئي، نظرية التابعية للكثافة، نظرية التابعية للكثافة التابعة للزمن، السوية الأرضية، السوية المثارة.

TD-DFT calcalution of BODIPYand related compunds as photoseners for Photodynamic therapy

B. Kamel[*] **Dr. W. Bachir**[**] **Dr. M. S. El-Daher**[***]

Abstract

In this work we carrid out Theoretical evaluation of Bodipy and related as photosensitizer for use in photodynamic therapy (PDT).Five compounds were studied through substituents at the position 6 in the chromophore of Bodipy with elements from the fifth column in the Periodic table such(N-P-As-Bi).in the present study the density functional theory and its time dependent extension calculations have been used to calculate the eneregy of ground and singlet -triplets excited states, energy differences $\Delta E_{T_1-S_0}$ $\Delta E_{S_1-T_1}$, electronic absorption spectra , transition dipole moments (TDM) for spin-allowed $S_0 \rightarrow S_n$ and other proporities.

---

[*] Higher Institute for laser Research and Applications, Damascus University, Syria
[**] Faculty of Informatics Engineering, Al-Sham Private university, Syria.
[***] Arab International university, Syria.

Keywords: Bodipy، photosenstizers، PDT، TD-DFT ،ground state، excited state.

1. Introduction

Photodynamic therapy (PDT) is a minimally invasive procedure that offers many advantages over traditional cancer treatments [1].

(PDT) was discovered more than 100 years ago, and has since become a well-studied therapy for cancer and various non-malignant diseases including infection[2].

It has been used for many years, but it is only now becoming widely accepted and utilized Originally it was developed as a tumor therapy and some of its most successful applications are for non-malignant diseases[3]. Photodynamic therapy employs light-sensitive compounds known as photosenstizers (PSs) that when exposed selectively to light in conjunction with molecular oxygen become toxic to cells resulting in cell death[1-3]. The process is initiated when the photosensitizer absorbs a photon and undergoes simultaneous or sequential decays that result in intramolecular energy transfer reactions[4].

after the photosensitizer absorbs light, it is activated to an excited singlet state. Molecules at this state readily decay back to the ground state with the emission of light (fluorescence) or heat, or they can cross to the triplet state[4]. The photosensitizer in the triplet state can react with ground-state oxygen to produce a singlet-state oxygen which is generally accepted as the major damaging species in PDT.

There are many types of photosensitizers available.

An ideal PS agent should be a single pure compound to allow quality control analysis with low manufacturing costs and good stability in storage. It should have a high absorption peak between 600 and 800 nanometers (nm) (red to deep red), because absorption of photons with wavelengths longer than 800 nm does not provide enough energy to excite oxygen to its singlet state and to form a substantial yield of reactive oxygen speciesoxygen species[5]. The first PS to be clinically employed for cancer therapy was a water-soluble mixture of porphyrins called hematoporphyrin derivative (HPD), a purified form of which, porfimer sodium, later became known as Photofrin. Although porfimer sodium is still the most widely employed PS, the product has some disadvantagesThe properties of unfavorable skin phototoxicity, low absorption in the red region of the visible spectrum, as well as complex mixtures arising from the method of synthesis were targeted for improvement with second generation photosensitizers.

There has been a major effort among medicinal chemists to discover second-generation PSs, and several hundred compounds have been proposed as potentially useful for anticancer PDT[6]. With several commercially available photosensitizing agents now on the market, numerous well designed clinical trials have demonstrated the efficacy of PDT on various cutaneous and deep tissue tumors. However, current photosensitizers and light sources still have a number of limitations[7-9]. Future PDT will build on those findings to allow development and refinement of more optimal therapeutic agents and illumination devices. 4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) derivatives have been proposed in several potential biomedical applications[8].

BODIPYs absorb strongly in blue-green region with high fluorescence emission, properties that convert them in effective fluorophores in the field of biological labeling. However, BODIPY structures can be conveniently modified by heavy atoms substitution to obtain photosensitizers with applications in photodynamic therapy .

BODIPYs have been proposed as phototherapeutic agents for the photodynamic inactivation of microorganisms[9].

Therefore, BODIPY structures need to be optimized to produce an efficient photocytotoxic activity.

BODIPY can be tuned from wavelengths (excitation and emission) of about ~500 nm to NIR wavelengths by structural modification with sharp absorption and emission bands. In addition to the flexible synthesis, several photophysical properties, such as singlet–triplet state character and electrochemical properties, can be tuned as desired.

These properties have enabled the transformation of a fluorescent dye with negligible triplet state to a PS[10].

BODIPY dyes tend to be highly fluorescent, but their emissions can be attenuated by adding substituents with appropriate oxidation potentials. Substituents like these have electrons to feed into photoexcited BODIPYs, quenching their fluorescence, thereby generating relatively long-lived triplet states. Singlet oxygen is formed when these triplet states interact with $^3O_2$ this causes cell death[11]. The PDT agents that are currently approved for clinical use do not feature BODIPYs, but there are many reasons to believe that this situation will change[12].

2-Computational details:

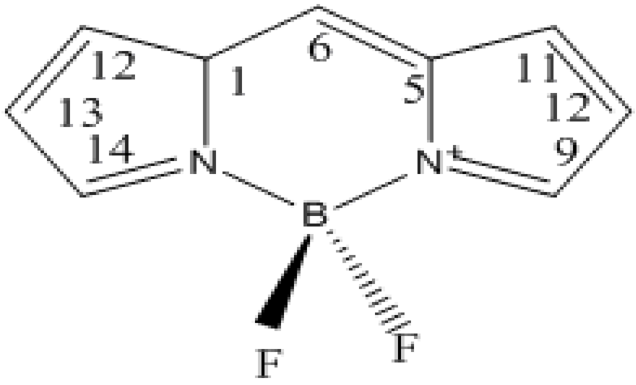
In the present work quantum mechanical calculations of Bodipy dye as photosensitizer were performed by DFT–TD-DFT which is One of the most powerful methods for theoretical studying of spectroscopic properties of large molecular systems.by using hybrid functional (B3LYP) the most commonly used not only for ground-state but also for excited state calculations and basis set(6-31G, lanl2dz) [13-14].

The presence of solution affects the optical activity of molecular systems. The solute- solution interactions have a direct and significant influence on the UV-VIS spectra. As a consequence a reliable theoretical study of electronic spectra cannot be performed without a proper treatment of solution effects. The polarizable continuum model (PCM) is one of the most widely used methods since it meets a good compromise between accuracy and computation time[15-16].

the present work present study for five compounds four of it dervited from chromophore Bodiby by substituents carcon number 6 by atoms from the fifth column in the Periodic table (N-P-As-Bi) as shown in figure (1) and table(1).

The molecules were drawn using CHEM BIO software and theoretical calculation carried out by Gaussian 09 software The theoretical calculations were focused on the ground state by DFT .

the excited triplet and singlet states by TD-DFT[13].



Fig(1) Molecular structure of the BODIPY dye and the related compounds

Table (1): the five molecules

PM-6	PM-C	PM-N	PM-P	PM-As	PM-Bi

3-Results and discussion
3-1Geometry

The ground and excited-state structural parameters of Bodipy and studied I,II,III,IV- V compounds were obtained by using calculations by DFT/ B3LYP/6-31G (lanl2dz for Bi) Bond length, Bond angles and Dihedral angles are presented in tables (2,3,4) respectively. It was shown abiggiest increase in the bond length C5-C6 when substituted with Bi in (C5-Bi6) And abiggiest increase in the bond length C1-C6 when substituted with Bi in(C1-Bi6).

For the Bond angles in the table(3) it was shown in the bond C5-(X)6 – C1smallest value in the presence of Bi Table(4) was shown biggest change in the values of Dihedral angles at Bi.

Table(2): Bond length (A) for PM for ground state

	Atoms	Actual	Optima	
PM-C	C(5)-C(6)	1.3924	1.523	
	N(4)-C(9)	1.3519	1.438	
	N(4)-C(5)	1.4084	1.438	
	B(3)-F(8)	1.4253		
	B(3)-F(7)	1.4253		
	B(3)-N(4)	1.5569		
	N(2)-C(14)	1.3519	1.438	
	N(2)-B(3)	1.5569		
	C(1)-C(6)	1.3924	1.523	
	C(1)-N(2)	1.4084	1.438	
PM-N	C(5)-N(6)	1.4004	1.456	
	N(4)-C(9)	1.3757	1.364	
	N(4)-C(5)	1.3814	1.364	
	B(3)-F(8)	1.5462		
	B(3)-F(7)	1.5451		
	B(3)-N(4)	1.5038		
	N(2)-C(14)	1.3142	1.47	
	N(2)-B(3)	1.5013		
	C(1)-N(6)	1.2902	1.26	
	C(1)-N(2)	1.4499	1.462	
PM-P	C(5)-P(6)	1.773	1.828	
	N(4)-C(9)	1.3569	1.364	
	N(4)-C(5)	1.4034	1.364	
	B(3)-F(8)	1.4238		
	B(3)-F(7)	1.429		
	B(3)-N(4)	1.5523		
	N(2)-C(14)	1.3569	1.364	
	N(2)-B(3)	1.5523		
	C(1)-P(6)	1.773	1.828	
	C(1)-N(2)	1.4034	1.364	
PM-As	C(5)-As(6)	1.8457		
	N(4)-C(9)	1.3575	1.364	

	N(4)-C(5)	1.3989	1.364	
	B(3)-F(8)	1.4304		
	B(3)-F(7)	1.4242		
	B(3)-N(4)	1.5513		
	N(2)-C(14)	1.3574	1.364	
	N(2)-B(3)	1.5515		
	C(1)-As(6)	1.8457		
	C(1)-N(2)	1.3991	1.364	
PM-Bi	C(5)-Bi(6)	2.1148		
	N(4)-C(9)	1.3693	1.364	
	N(4)-C(5)	1.4081	1.364	
	B(3)-F(8)	1.4338		
	B(3)-F(7)	1.4462		
	B(3)-N(4)	1.5473		
	N(2)-C(14)	1.3691	1.364	
	N(2)-B(3)	1.5476		
	C(1)-Bi(6)	2.1145		
	C(1)-N(2)	1.408	1.364	

Table(3) Bond angles ( )0for PM for ground state

	Atoms	Actual	Optimal
PM-C	C(5)-C(6)-C(1)	121.7616	109.5
	C(6)-C(5)-N(4)	120.4047	108.8
	C(5)-N(4)-B(3)	125.4343	
	F(8)-B(3)-F(7)	109.6157	
	N(4)-B(3)-N(2)	106.5603	
	B(3)-N(2)-C(1)	125.4343	126
	C(6)-C(1)-N(2)	120.4047	108.8
PM-N	C(5)-N(6)-C(1)	113.7233	115
	N(6)-C(5)-N(4)	126.3373	126
	C(5)-N(4)-B(3)	117.3263	108.8
	F(8)-B(3)-F(7)	109.4223	107.7
	N(4)-B(3)-N(2)	105.1088	
	B(3)-N(2)-C(1)	116.5427	
	N(6)-C(1)-N(2)	124.7189	126
PM-P	C(5)-P(6)-C(1)	100.7827	115
	P(6)-C(5)-N(4)	125.3269	126

	C(5)-N(4)-B(3)	126.9616	108.8
	F(8)-B(3)-F(7)	109.9763	107.7
	N(4)-B(3)-N(2)	108.7463	
	B(3)-N(2)-C(1)	126.9611	
	P(6)-C(1)-N(2)	125.3256	126
PM-As	C(5)-As(6)-C(1)	98.7024	115
	As(6)-C(5)-N(4)	125.1495	126
	C(9)-N(4)-C(5)	108.2799	124
	C(5)-N(4)-B(3)	126.565	108.8
	F(8)-B(3)-F(7)	110.149	107.7
	B(3)-N(2)-C(1)	126.5945	
	As(6)-C(1)-N(2)	125.1118	126
PM-Bi	C(5)-Bi(6)-C(1)	92.3833	115
	Bi(6)-C(5)-N(4)	123.9002	126
	C(9)-N(4)-B(3)	123.578	108.8
	C(5)-N(4)-B(3)	127.1633	108.8
	F(8)-B(3)-F(7)	109.6948	107.7
	C(12)-C(1)-Bi(6)	128.176	120
	Bi(6)-C(1)-N(2)	123.9194	126

Table (4): Dihedral angles( )0 of PM for ground state

	Atoms	Actual
PM-C	N(2)-C(1)-C(6)-C(5)	0.0000
	B(3)-N(4)-C(5)-C(11)	179.9966
PM-N	N(2)-C(1)-N(6)-C(5)	10.3514
	B(3)-N(4)-C(5)-C(11)	150.1226
PM-P	N(2)-C(1)-P(6)-C(5)	2.3375
	B(3)-N(4)-C(5)-C(11)	171.2981
PM-As	N(2)-C(1)-As(6)-C(5)	5.1103
	B(3)-N(4)-C(5)-C(11)	169.5953

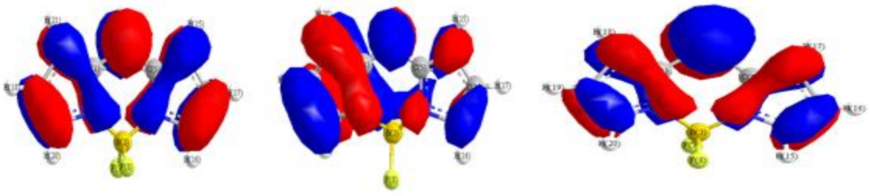
PM-Bi	N(2)-C(1)-Bi(6)-C(5)	5.3297
	B(3)-N(4)-C(5)-C(11)	168.7146

3-2Absorption:

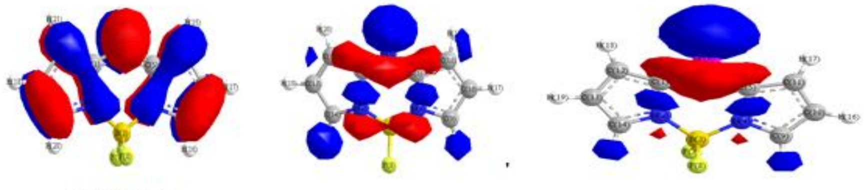
absorption bands was obtained by using TD-DFT/B3LYP/ PCM/6-31G (lanl2dz for Bi) in isolated gas phase and solutions Acetonitrile, Ethanol,and DMSO it was shown biggest absorption band in the atom Bi and the acetonitrile as shown in the table (5)

Table(5): The calculation absorption bands of PM by TD-DFT/B3LYP/ PCM/6-31G (lanl2dz for Bi) in Acetonitrile, Ethanol, DMSO solutions

PM	PM-C	PM-N	PM-P	PM-As	PM-Bi
λ_{abs} (nm)	415,98	475,46	556,69	525,36	609,63
λabs (nm) Acetonitrile	420,72	477,88	489,33	518,94	569,63
λabs (nm) Ethanol	421	478,48	490,19	521,62	570,91
λabs (nm) DMSO	422,91	479,83	491,84	521,62	571,79



IUMO-PM-C IUMO-PM-N LUMO-PM-P



HOMO-PM-c HOMO-PM-N HOMO-PM-P

LUMO-PM- As LUMO-PM- Bi

HOMO-PM-As HOMO-PM-Bi

Fig (2): HOMO and LUMO states for all studied compounds.

Tables (6-7-8) show calculations of oscillator strengths (*f*) and transition dipole moments (TDM) of the spin-allowed S0→Sn in Acetonitrile, Ethanol, DMSO solutions.

Table(6): The parameters of the transition dipole moments (TDM)
for spin-allowed S0→Sn, oscillator strengths (f).
TD-DFT/B3LYP/ PCM/6-31G (lanl2dz for Bi) in Ethanol solution

Ethanol	$S_0 \to S_n$	TDM [a.u]				MO	
		d_x	dy	dz	Dip		f [a.u.]
PM-C	$\to S_1$	2.2	0.2	-0.0	4.9	H-0→L+0 (91%)	0.2917
	$\to S_2$	0.4	0.2	0.0	0.2	H-1→L+0 (90%)	0.0170
	$\to S_3$	0.3	0.3	-0.3	0.3	H-2→L+0 (96%)	0.0327
PM-N	$\to S_1$	1.9	-0.7	0.0	4.2	H-0→L+0 (71%)	0.2283
	$\to S_2$	0.5	0.6	-0.0	0.67	H-1→L+0 (70%)	0.0440
	$\to S_3$	-0.3	-0.5	0.0	0.4	H-3→L+0 (64%)	0.0318
PM-P	$\to S_1$	2.2	0.0	-0.0	4.9	H-0→L+0 (80%)	0.3046
	$\to S_2$	1.4	−0.2	-0.0	2.1	H-1→L+0 (78%)	0.1442
	$\to S_3$	-0.2	-0.2	0.0	0.1	H-2→L+0 (92%)	0.0113
PM-As	→S1	2.2	0.2	-0.0	4.9	H-0→L+0 (98%)	0.2917
	→S2	0.4	0.2	0.0	0.2	H-1→L+0 (97%)	0.0170
	→S3	0.3	0.3	-0.3	0.3	H-3→L+0 (51%)	0.0327
PM-Bi	→S1	1.9	-0.7	0.0	4.2	H-0→L+0 (99%)	0.2283
	→S2	0.5	0.6	-0.0	0.6	H-1→L+0 (64%)	0.0440
	→S3	-0.3	-0.5	0.0	0.4	H-0→L+0 (71%)	0.0318

Table(7): The parameters of the transition dipole moments (TDM)
for spin-allowed $S_0 \rightarrow S_n$, oscillator strengths (f).
TD-DFT/B3LYP/ PCM/6-31G (lanl2dz for Bi) in DMSO solution

DMSO	$S_0 \rightarrow S_n$	TDM [a.u]				MO	
		d_x	dy	dz	Dip		f [a.u.]
PM-C	→S_1	2.4	0.0	0.1	5.8	H-0→L+0 (92%)	0.4178
	→S_2	-1.1	0.3	0.0	1.4	H-1→L+0 (91%)	0.1179
	→S_3	-0.5	-0.6	0.0	0.7	H-2→L+0 (96%)	0.0797
PM-N	→S_1	1.9	0.0	0.0	3.8	H-0→L+0 (73%)	0.2433
	→S_2	-1.7	0.3	-0.0	3.1	H-1→L+0 (72%)	0.2238
	→S_3	-0.5	-0.2	0.1	0.4	H-3→L+0 (63%)	0.0368
PM-P	→S_1	2.2	-0.0	-0.0	5.2	H-0→L+0 (83%)	0.3256
	→S_2	1.3	-0.2	-0.0	1.9	H-1→L+0 (81%)	0.1314
	→S_3	-0.2	-0.2	0.0	0.1	H-3→L+0 (92%)	0.0116
PM-As	→S1	2.2	0.2	-0.0	5.1	H-0→L+0 (99%)	0.2982
	→S2	0.4	0.3	0.0	0.2	H-1→L+0 (67%)	0.0165
	→S3	0.3	0.3	-0.3	0.3	H-2→L+0 (96%)	0.0336
PM-Bi	→S1	1.9	-0.7	0.0	4.3	H-0→L+0 (`98%)	0.2335
	→S2	0.5	0.6	-0.0	0.7	H-1→L+0 (97%)	0.0482
	→S3	0.3	-0.5	0.0	0.4	H-3→L+0 (51%)	0.0301

Table(8): The parameters of the transition dipole moments (TDM) for spin-allowed $S_0 \to S_n$, oscillator strengths (f).
TD-DFT/B3LYP/ PCM/6-31G (lanl2dz for Bi) in acetonitrile solution

acetonitrile	$S_0 \to S_n$	TDM [a.u]				MO	
		d_x	dy	dz	Dip		f [a.u.]
PM-C	$\to S_1$	2.3	0.0	0.1	5.5	H-0→L+0 (91%)	0.4009
	$\to S_2$	-1.1	0.3	0.0	1.4	H-1→L+0 (90%)	0.1222
	$\to S_3$	-0.5	-0.6	0.0	0.7	H-2→L+0 (95%)	0.0778
PM-N	$\to S_1$	1.8	0.0	0.0	3.5	H-0→L+0 (71%)	0.2259
	$\to S_2$	-1.7	0.3	-0.0	3.1	H-1→L+0 ((70%)	3.1728
	$\to S_3$	-0.5	-0.2	0.1	0.4	H-3→L+0 (64%)	0.0362
PM-P	$\to S_1$	2.1	0.0	-0.0	4.8	H-0→L+0 (39%)	0.3002
	$\to S_2$	1.4	-0.2	-0.0	2.1	H-1→L+0 (77%)	0.1459
	$\to S_3$	-0.2	-0.2	0.0	0.1	H-2→L+0 (92%)	0.0114
PM-As	→S1	2.2	0.2	-0.0	4.9	H-0→L+0 (98%)	0.2894
	→S2	0.4	0.2	0.0	0.2	H-1→L+0 (97%)	0.0170
	→S3	0.3	0.3	-0.3	0.3	H-3→L+0 (52%)	0.0321
PM-Bi	→S1	1.9	-0.7	0.0	4.2	H-0→L+0 (99%)	0.2264
	→S2	0.5	0.6	-0.0	0.6	H-1→L+0 (32%)	0.0442
	→S3	-0.3	0.5	0.0	0.4	H-2→L+0 (66%)	0.0306

3-3Triplet energy:

Triplet energy are regarded to be responsible for the efficiency of photosensitizers in PDT. To be interesting for PDT, the first excited state of the photosensitizer (S_1, 1PS*) should be triggered by light with an energy of between 1.55 eV (800 nm) and 1.77 eV (700 nm). This range is predicted to provide at the same time the deepest penetration depth into biological tissue and enough triplet energy (T_1, 3PS*) to produce singlet oxygen. Among investigated structures the compound PM-bi have such properties as shown in table (9).

Table(9): energy differences$\Delta E_{T_1-S_0}$ $\Delta E_{S_1-T_1}$by DFT/B3LYP/ /6-31G \(lanl2dz for Bi)for ground states and TD-DFT/B3LYP/ /6-31G (lanl2dz for Bi)for excited states

PM	PM-C	PM-N	PM-P	PM-As	PM-Bi
$\Delta E_{T_1-S_0}$	3	2,50	2.67	2,15	1,96
$\Delta E_{S_1-T_1}$	3,14	2,66	1,90	1,81	1,56

Conclusion

Theoretical calculations were performed for five compounds by using density functional theory (DFT) and time-dependent density functional theory (TDDFT)in isolated gas phase and solutions Acetonitrile, Ethanol, and DMSO . through the polarizable continuum model (PCM).

The foregoing studies indicate that PM-Bi was best compound as photosensitizers in pdt.

Future research should be aimed at synthesis of promising compounds such PM-Bi,PM-AS,PM-P for photodynamic therapy and executing experiments to verify the correctness of the theoretical results.

References:

1-Cai-Hua Zhou, Xiang Zhao, Theoretical investigation on quinoline-based platinum (II) complexes as efficient singlet oxygen photosensitizers in photodynamic therapy. Journal of Organometallic Chemistry 696 (2011) 3322e3327.

2-AT Byrne, AE O'Connor, M Hall, J Murtagh, K O'Neill, KM Curran, K Mongrain, JA Rousseau, R Lecomte, S McGee, JJ Callanan, DF O'Shea and WM Gallagher, Vascular-targeted photodynamic therapy with BF2-chelated Tetraaryl-Azadipyrromethene agents: a multi-modality molecular imaging approach to therapeutic assessment. British Journal of Cancer (2009) 101, 1565 – 1573.

3-Samuel G. Awuahab and Youngman You, Boron dipyrromethene (BODIPY)-based photosensitizers for photodynamic therapy. The Royal Society of Chemistry (2012) 10.1039/c2ra21404k.

4-Maria J. Ortiz , Antonia R. Agarrabeitia , Gonzalo Duran-Sampedro, Jorge Ba~nuelos Prieto , Teresa Arbeloa Lopez, Walter . Massad , Hern_an. Montejano , Norman A. García c, I~nigo Lopez Arbeloa , Synthesis and functionalization of new polyhalogenated BODIPY dyes. Study of their photophysical properties and singlet oxygen generation. Tetrahedron 68 (2012) 1153e1162.

5-Mohammad R. Momeni and Alex Brown, Why Do TD-DFT Excitation Energies of BODIPY/Aza-BODIPY Families Largely Deviate from Experiment? Answers from Electron Correlated and Multireference Methods, Journal of Chemical Theory and Computation(2014) 10.1021/ct500775r.

6-Yusuf Cakmak, Safacan Kolemen, Selig Duman, Yavuz Dede, Yusuf Dolen, Bilal Kilic, Ziya Kostereli, Leyla Tatar Yildirim, A. Lale Dogan, Dicle Guc, and Engin U. Akkaya, Designing Excited States: Theory-Guided

Access to Efficient Photosensitizers for Photodynamic Action. Angew. Chem. 2011, 123, 12143 –12147.

7-Soumyaditya Mula, Alok K. Ray, Manas Banerjee, Tandrima Chaudhuri, Kamalesh Dasgupta, and Subrata Chattopadhyay, Design and Development of a New Pyrromethene Dye with Improved Photostability and Lasing Efficien.cy: Theoretical Rationalization of Photophysical and Photochemical Properties. *J. Org. Chem.* 2008, *73*, 2146-2154.

8-Bruna Clara De Simone, Gloria Mazzone , Nino Russo, Emilia Sicilia and Marirosa Toscano, Metal Atom Effect on the Photo physical Properties of Mg(II), Zn(II), Cd(II), and Pd(II) Tetraphenylporphyrin Complexes Proposed as Possible Drugs in Photodynamic Therapy. *Molecules* 2016, *21*, 1093.

9- C.H. Sabot, V.C. Colusa, N.L. Oleinick and T.J. Kinsella, Photodynamic therapy: a new concept in medical treatment. Braz J Med Biol Res 33(8) 2000.

10- Juan L. Vivero-Escoto, Daniel DeCillis, Laura Fritts and Daniel L. Vega1, Porphyrin-based polysilsesquioxane nanoparticles to improve photodynamic therapy for cancer treatment.(2015) Proc. of SPIE Vol. 8931 89310Z-1.

10- Zu-De Qi, Dong-Wei Li, Peng Jiang,a Feng-Lei Jiang,a Yue-Sheng Li,ab Yi Liu, Wai-Kwok Wong and Kok-Wai Chee, Biocompatible CdSe quantum dot-based photosensitizer under two-photon excitation for photodynamic therapy J. Mater. Chem., 2011, 21, 2455–2458 | 2455.

11- Gal Shafirstein , David Bellnier , Emily Oakley , Sasheen Hamilton , Mary Potasek , Karl Beeson and Evgueni Parilov, Interstitial Photodynamic Therapy—A Focused Review. Cancers 2017, 9, 12; doi:10.3390/ cancers9020012.

12- Institute of Material Science and Applied Research, Vilnius, Lithuania, Photodynamic therapy: mechanism of action and ways to improve the efficiency of treatment. MEDICINA (2003) 39 tomas, Nr. 12.

13- Muhammad Raziq Rahimi Kooh, Voo Nyuk Yoong and Piyasiri Ekanayake, Density functional theory (DFT) and time-dependent density functional theory (TDDFT) studies of selected ancient colourants as sensitizers in dye-sensitized solar cells.(2014) Journal of the National Science Foundation of Sri Lanka 42(2).

14- Shidang Xu,Youyong Yuan, Xiaolei Cai,a Chong-Jing Zhang,a Fang Hu,b Jing Liang,a Guanxin Zhang,b Deqing Zhangb and Bin Liu. Tuning the singlet-triplet energy gap: a unique approach to efficient photosensitizers with aggregation-induced emission (AIE) characteristics. The Royal Society of Chemistry 2015.

15- AlexandraB. Ormond and Harold S. Freeman, Dye Sensitizers for Photodynamic Therapy. Materials 2013, 6, 817-840; doi:10.3390/ ma6030817.

16- Keenan Komoto Research Advisor: Dr. Tim Kowalczyk, A Computational Approach to Studying the Properties of Photosensitizers in Photodynamic Therapy.