Role of Coordination compounds as photosensitizes of photodynamic therapy :on overview

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Abstract

Photodynamic therapy (PDF) is a good method to treat types of cancer such as skin cancer. This method depends on the properties of the dye sensitizers. We focused on the dye metal complexes because they absorb in visible to infra-red area with high intersystem crossing which is important condition to occur PDT. The dye metals complexes of boron-dipyrrin , pyridyl, chlorins, bacteriophorbides, texaphlins and phthalocyanines dyes exhibited low toxicity in dark condition, absorption in visible to infrared area, high toxicity under irradiation for many diseases of cancer, various, and bacteria.

Keywords: Photodynamic therapy, boron-dipyrrin, *cancer*, dye sensitizers

Introduction

Photodynamic therapy (PDT) is an important method in medicine which includes applying the light on a photosensitizer in environment of oxygen to produce reactive oxygen species (ROS or $^1O_2$) which induces cellular and tissue damage [1, 2].

Photodynamic therapy (PDT) uses to treat varions types of cancer, bacterial infections, viral, viruses[3] and fungal. We are interesting in metal complexes as photosensitizers in photodynamic therapy more than organic compounds which suffer hard soluble in water, low photostability, aggregation, and long time of excretion. Metal-based drugs have large area useful for therapeutic and diagnostic purposes [4–6]. One of the advantages of treatment PDT, the photosensitizing dyes accumulation in tumour tissue are more than in normal tissue, the damages of PDT are locally in the irradiated area.

The PDT uses also to treat the viruses such as Zika virus, SARS coronavirus, immunodeficiency viruses (AIDS). Figure 1 presents principles steps of DFT and the reactive species attract RNA, DNA,

proteins and lipids in viruses, cancer cells and bacteria [7].

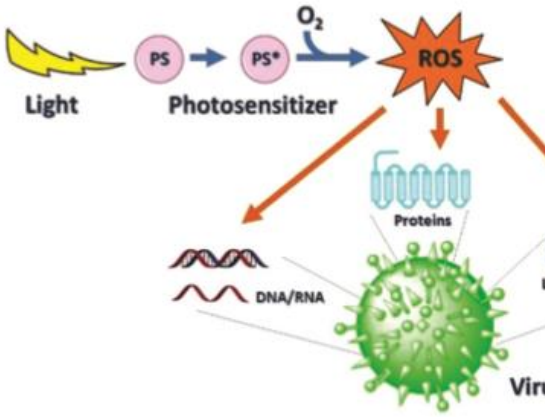

Figure 1 Targets of Photodynamic therapy of viruses included nucleic acids, proteins and lipids [7]

The light used in the PDT depends on the maximum absorption of the dye, preferably with a high wavelength close to the infrared area where its penetration in the tissues is greater and its damage is less on the tissues [8–10]. Therefore now a two-photon absorption technique is used which is nonlinear optic. The wavelength in this technic is double the wavelength in the case of absorption of one photon which permits to penetrate the light more in the tissue with less damage (Figure 2) [11–13].

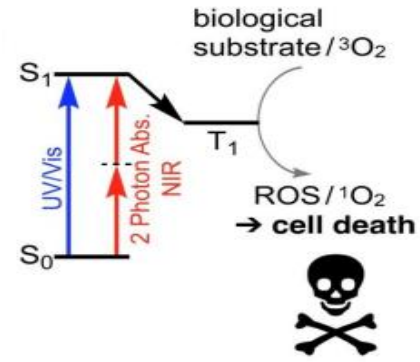

Figure 2 Excitation mechanism of dye sensitizers [2]

Boron-dipyrrin complexes (BODIPYs) show featured properties such as the absorption/emission and high chemical stability. These complexes use in various fields such as bioimaging, sensors, and solar cells and a photosensitizing effect in photodynamic therapy [14].

The complexes of BODIPYs having heavy atoms are better as a photosensitizing effect which increase their applicable as anticancer photodynamic therapy[15]. These dyes are suitable for DFT agents due to low dark toxicities, cellular uptake, high extinction coefficients, and low quantum yields for photobleaching.

Dipyrrin derivative of ((Z)-3-iodo-5-((4-iodo-3,5-dimethyl-2H-pyrrol-2-ylidene)(mesityl)methyl)-2,4-dimethyl-1Hpyrrole)complex of Cu(II) and Ni(II) (Figure 3) exhibited potential role in PDT to treat human cervical carcinoma (HeLa) cells at irradiation light under 510 nm [16].

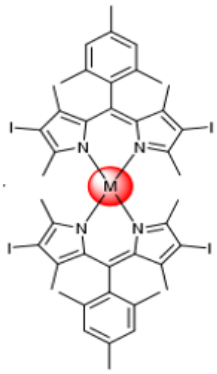

Figure 3 Dipyrrin derivative with metal ions (M= Cu(II) or Ni(II))

The substituted boron dipyrrin (BODIPY) of selenophene (Figure 4) are good fluorophores and photosensitizers. They used to yield singlet oxygen [17].

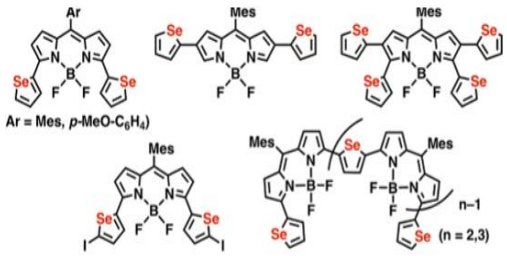

Figure 4 Boron dipyrrin (BODIPY) of selenophene

The thiophene units in the BODIPY (Figure 5) exhibited significant effects such as long triplet lifetimes, detraction extinction coefficients and better absorption and fluorescence maxima [18].

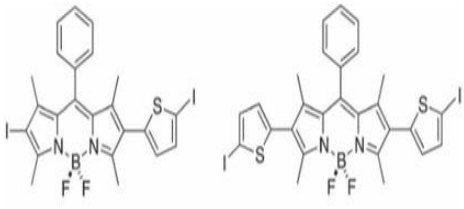

Figure 5 The thiophene units in the BODIPY

The macrocyclic series ligands of BODIPY (Figure 6) with Pd(II), Ru(II) and Ir(III) exhibited triangular geometries in the polar solvent such as methanol, acetone while mixture geometries (triangular and square) in low polar solvents like CH_2Cl_2 and chloroform. These supramolecules of BODIPYs exhibited strongly interaction with biomolecules, such as proteins and DNA, and a selective citotoxicity like against brain cancer cells, and aggregation-induced emission properties [19–21].

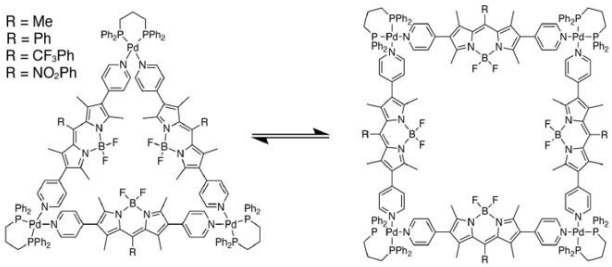

Figure 6 The macrocyclic series ligands of BODIPY having palladium ion in dynamic equilibrium between triangular and square shapes

Many pyridyl ligands such as bipyridine, phenanthroline and their substituents of ruthenium (Figure 7) exhibited ability to generate $^1O_2$ accomping with yields up to 94% in acetonitrile while in phosphate buffered saline up to 6% that means that the quantum yields of $^1O_2$ depend on the nature of solvent.

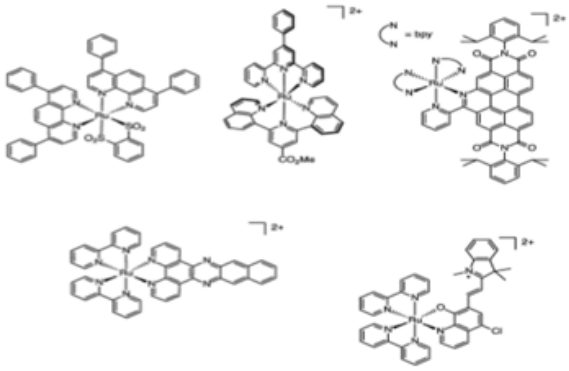

Figure 7 Pyridyl ruthenium complexes exhibit high generate singlet oxygen

The complexes 1, 2 (Figure 8) of pyrdyl derivatives exhibited ability to generate $^1O_2$ with quantum yield 75% and 54% respectively in acetonitrile. Under one photon irradiation at 400 nm, the complexes

1, 2 exhibited IC_{50}= 3.1 μM and 16.7 μM respectively while under two-photon irradiation at 800 nm the complexes 1rxhibted IC_{50}= 9.5 μM towards HeLa cells [22].

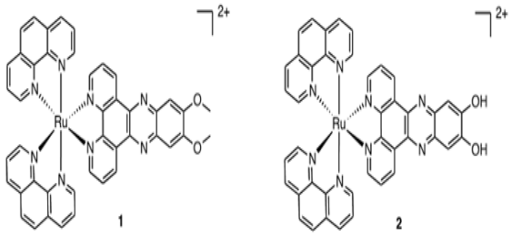

Figure 8 Ruthenium complexes phenanthroline derivatives

The supramolecular hetero-metallic Ru–Pt metallacycle (Figure 9) exhibited good photostability with larger two-photon absorption cross-section which is due to Ru(II) polypyridyl precursor and high generation efficiency of singlet oxygen [23]. The metallacycle was noticed having selectively accumulates in mitochondria and nuclei upon internalization which leads to damage for mitochondrial function and intranuclear DNA.

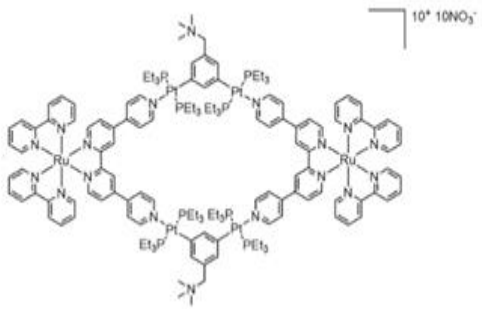

Figure 9 Metallacycle complexes of Ru-Pt

Ruthenium-azo ligand (4,4``-azobis(2,2`-bipyridine) (Figure 10) exhibited excellent photodynamic anticancer agent toward HeLa, A549 and LO2 cells [24].

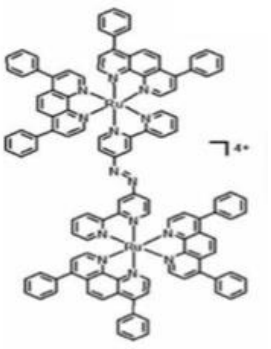

Figure 10 Azo dye of ruthenium pyridyl complex

Porphyrinoid complexes photosensitizers

The important classes of tetrapyrroles are porphyrins, chlorins and bacteriochlorins which are depectied in figure (11) in blue, green and red colors respectively.

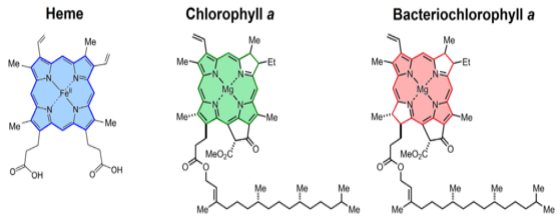

Figure 11 Chemical structures of heme, chlorophyll a, and bacteriochlorophyll a

The derivatives of chlorin e_6 dimethyl ether (methylpyropheophorbide a, and exocycle-free 13-amide) with copper (II) (Figure 12) was formed by chemical modification of chlorophyll a. They exhibited low toxicity at dark condition, increasing generation singlet oxygen. They exhibited suitable behaviour as photosensitizer against HeLa celles line [25].

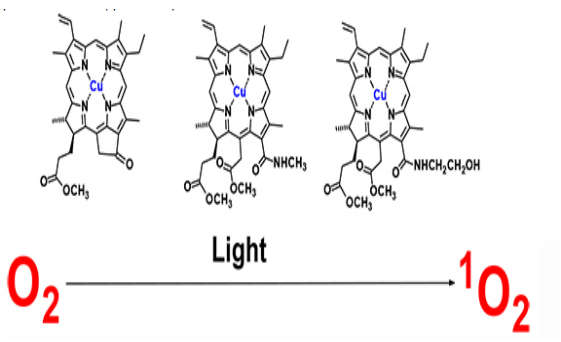

Figure 12 The derivatives of chlorin e_6 dimethyl ether with copper ion, increasing generation singlet oxygen from left to right

There is no high difference between bacteriopheophorbides and bacteriochlorins just the first has four hydrogens more than bacteriochlorins. Bacteriopheophorbides exhibit absorption at 740-800 nm with high molar extinction around 50000 $M^{-1}.cm^{-1}$. This absorption is consider a red shift corresponding to bacteriochlorins.

Padoporfin (Tookad®) is amportant dye for bacteriupheophorbides which is derived from bacteriochlorphyll a as shown in figure 13. This dye is activated under 763 nm, it has low skin accumulation and deeper tissue penetration. Another advantage for this dye has minimum skin photosensitivity.

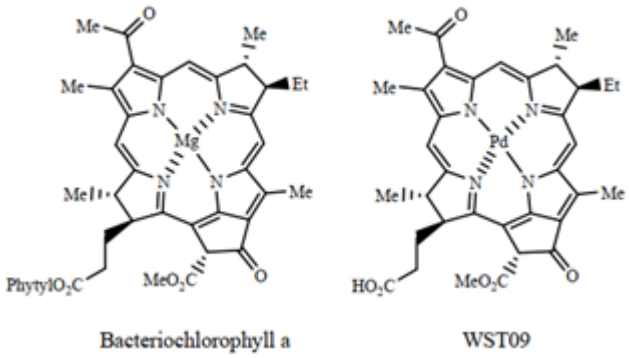

Figure 13 Bacteriochlorphyll a and Padoporfin (WST09)

Texaphrins: The best example on texaphrins is Lu-Tex drug (Lutrin®) Figure 14 which has pentaaza core. This dye is soluble in water and it absorbs the light at 732 nm with molar extinction around 42000 $M^{-1}.cm^{1-}$. This drug used to treat prostate cancer, breast cancer and malignant melanoma [26, 27].

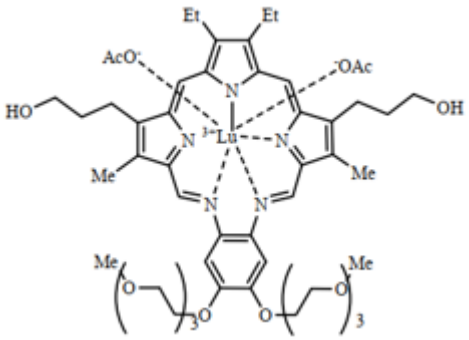

Figure 14 Texaphrin complex of lutetium ion

Phthalocyanines exhibit high intense blue-green colour, absorb in the region of 650-700 nm with extinction coefficients greater than 10^5 $M^{-1}.cm^{-1}$.[28, 29] The metal complexes of these dyes exhibit good photodynamic therapy properties because of transition metals allowing for

intersystem crossing which is important condition to occur PDT [30]. Silicon (IV) phthalocyanine as shown in figure 15 is soluble in water which leads to prevent the complex of silicon from aggregation. This dye used to treat the B16 melanoma cells under irradiation at 690 nm in aqueous solution while it did not exhibit toxicity at dark conditions .

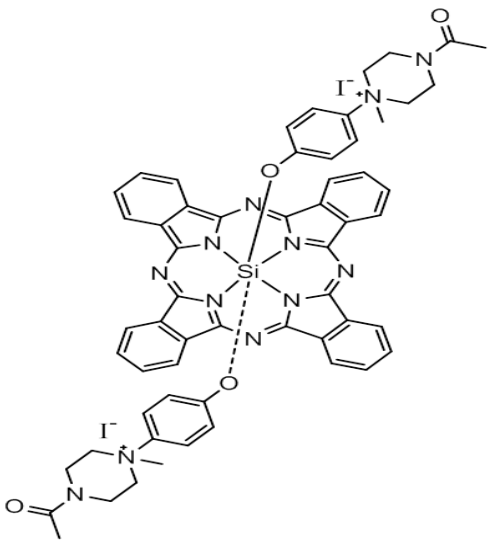

Figure 15 Water soluble complex of silicon (IV) phthalocyanine

Conclusion

Photosensitizers play essential role in treatment many diseases by using photodynamic therapy. The best photosensitizer which gives λ_{max} in the red region, high yield of ROS and $^1O_2$, having long lifetime at the triplet state. Photosensitizers under appropriate light become activated to treat cancer, viruses, eczema, vitiligo, and different types of bacteria. Boron-diprin complxex, Ruthenium pyridyl complexes, porphyrinoid complexes, texaphrin of lutetium and phthalocyanine complexes exhibited promising results as phtosensitizers in photodynamic therapy method.

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