Supplemantary Material

1. Materials and methods

1.1. Singlet oxygen quantum yields

The singlet oxygen quantum yields (Φ_Δ) of newly synthesized non-peripheral substituted phthalocyanines were measured according to the literature[1,2]. Φ_Δ was performed in air and at room temperature by using un-substituted ZnPc as a reference and 1,3-diphenylisobenzofuran (DPBF) as a chemical quencher. UV-Vis spectra were recorded, showing a decrease in the DPBF absorbance peak at approximately 417 nm. Φ_Δ was calculated by using equation 1.

$$\Phi_\Delta = \Phi_\Delta^{Std} \frac{R \,.\, I_{abs}^{Std}}{R^{Std} \,.\, I_{abs}} \quad (1)$$

In this equation, Φ_Δ^{Std} is the singlet oxygen quantum yield of the reference sample. The standard ZnPc (0.67 in DMSO and 0.56 for ZnPc in DMF, and 0.53 for ZnPc in THF)[3–5]. R and R_{Std} are the photobleaching rates of DPBF in the presence of non-peripheral substituted phthalocyanines and unsubstituted zinc phthalocyanines as a reference. I_{abs} and I_{abs}^{Std} are light absorption rates in the presence of the newly synthesized phthalocyanine and unsubstituted ZnPc.

1.2. Antioxidant activities

Antioxidant activities of the synthesized molecules were analyzed by using DPPH (2,2-Diphenyl-1-Picrylhydrazyl) radical scavenging and reducing power assays[6,7]. In DPPH assay, tested molecules and Trolox (positive control) were prepared at different concentrations ranging from 100 to 500 mg/mL. The DPPH radical scavenging activity percentage was calculated by using the following formula:

Scavenging activity (%) = (A control-A sample)/A control x 100

where A control is the absorbance of the control reaction mixture, A sample is the absorbance of the sample.

Reducing power assay was the second method used for the determination of antioxidant activity. First, 1 mL of sample was mixed with 2.5 mL of 200 mM sodium phosphate buffer (pH 6.6) and 2.5 mL of 1% potassium ferricyanide, and the mixture was incubated at 50 °C for 20 min. Then, 2.5 mL of 10% trichloroacetic acid was added, and the mixture was centrifuged at 3000 rpm for 10 min. The upper layer (2.5 mL) was mixed with 2.5 mL of deionized water and 0.5 mL of 0.1% ferric chloride. Finally, the absorbance was measured at 700 nm using UV–VIS spectrophotometer. BHT was used as the control.

1.3. Antibacterial activity

All antimicrobial tests were carried out against *Escherichia coli* (ATCC 25922) and *Staphylococcus aureus* (ATCC 29213) microbial cultures. All studies were performed in the dark without light exposure. For disc diffusion method, bacterial suspensions adjusted to the 0.5 McFarland standards ($1.5x10^8$ CFU/mL of bacteria) by spectrophotometrically. Agar containing petri dishes were inoculated by using these suspensions to control the contamination of microbial cultures before the experiment. For the disc diffusion method, Mueller-Hinton Agar (MHA) was prepared, sterilized and 20 mL of MHA was poured into each petri dish. After solidification they were inoculated with prepared microbial suspensions[8]. Each blank disc was loaded with 20 µL of synthesized molecules at different concentrations. Loaded discs were put into the inoculated petri dishes. MHA containing petri dishes were incubated at 37°C for 18 hours and then the zone of inhibitions was measured and recorded.

1.4. MTT Assay

Cytotoxicity was evaluated by the 3-(4,5-dimethyl-2-thiazolyl)- 2,5-diphenyl-2H-tetrazolium bromide (MTT) colorimetric assay[9]. All experiments were performed with the initial concentration of 1×10^4 cells/well in 96-well microplates at 37 °C under 5% CO_2 and 95% humidity for 24 hours incubation. Subsequently, the cultured cells were treated with various concentrations of the compounds (50, 5, 0.5 µg/ml) and incubated for a further 72 h at 37 °C. At the end of 72 hours, 20 µl of MTT solution (from 2.5 mg/ml stock, Acros, USA) was

added to the cells and incubated for 4 hours at 37°C. Doxorubicin was used as a positive control. After 4 hours of incubation at 37°C, the medium was removed and 150 µL DMSO was added into each well and the optical density of the dissolved formazan crystals was measured at 570 nm (reference filter, 620 nm) with UV-Vis spectrophotometer (Thermo Fisher Scientific). The percentage of viability of cells in the treatment groups was calculated as the following formula:

% viable cells = [(absorbance of treated cells) - (absorbance of blank)] / [(absorbance of control) - (absorbance of blank)] × 100

IC_{50} values were calculated with GraphPad Prism software (version 5, GraphPad Software, La Jolla, CA, USA) for each cell line using the percentage of viability.

1.5. Theoretical methods

Theoretical calculations provide important information about the chemical and biological properties of molecules. Many quantum chemical parameters are obtained from theoretical calculations. The calculated parameters are used to explain the chemical activities of the molecules. Many programs are used to calculate molecules. These programs are Gaussian09 RevD.01 and GaussView 6.0[10,11]. By using these programs, calculations were made in B3LYP, HF, and M06-2x[12–14] methods with the 6-31++g(d,p) basis set. As a result of these calculations, many quantum chemical parameters have been found. Each parameter describes a different chemical property of molecules. The theoretical parameters are calculated as follows[15,16].

$$\chi = -\left(\frac{\partial \mathrm{E}}{\partial \mathrm{N}}\right)_{\upsilon(r)} = \frac{1}{2}(I + A) \cong \frac{1}{2}(E_{HOMO} + E_{LUMO})$$

$$\eta = -\left(\frac{\partial^2 \mathrm{E}}{\partial \mathrm{N}^2}\right)_{\upsilon(r)} = \frac{1}{2}(I - A) \cong -\frac{1}{2}(E_{HOMO} - E_{LUMO})$$

$$\sigma = 1/\eta \qquad \omega = \chi^2/2\eta \qquad \varepsilon = 1/\omega$$

A technique exists for contrasting the biological actions of the metal complexes with those of protein. Molecular docking is the most typical of them. Metal complexes can be compared using a few of these molecular docking techniques. HEX software is employed in this investigation. These proteins interact with the ligand and its metal complexes to boost their

biological activity[17]. Molecules' biological activities were compared to those of proteins using molecular docking calculations. At HEX 8.0.0, the protein and molecule files were examined[18,19]. For docking, the following variables are used: Correlation type shape only, 3D FFT mode, 0.6-dimensional grid, 180-degree receptor and ligand ranges, 360-degree twist range, and 40-degree distance range. The interaction between the chemicals and the proteins was also thoroughly examined using the Protein-Ligand Interaction Profiler (PLIP) service [20,21]. The interaction between the chemicals and the proteins was also thoroughly examined using the Protein-Ligand Interaction Profiler (PLIP) service.

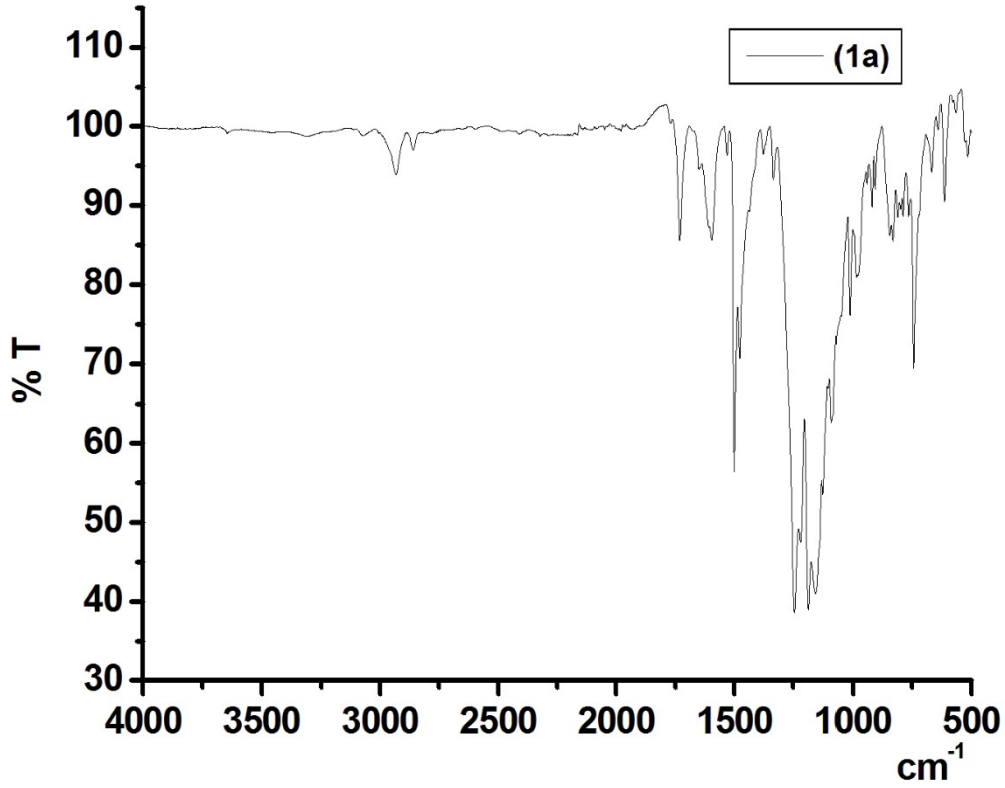

Fig. S1. FT-IR spectrum of the phthalocyanine **(1a)**

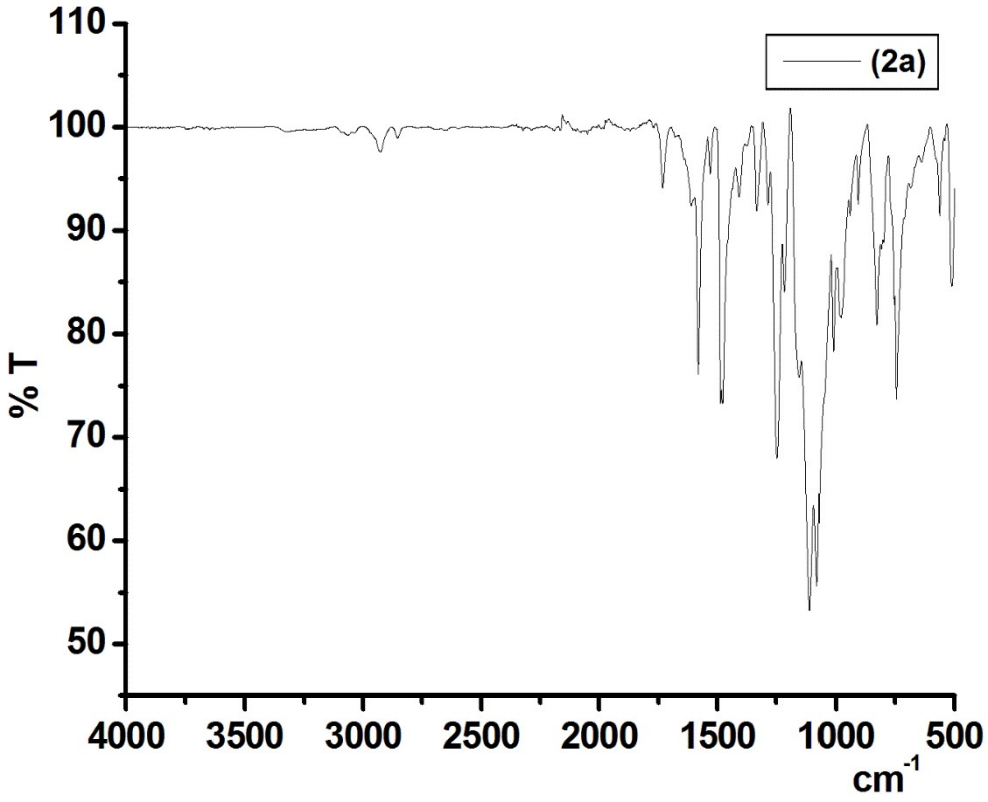

Fig. S2. FT-IR spectrum of the phthalocyanine **(2a)**

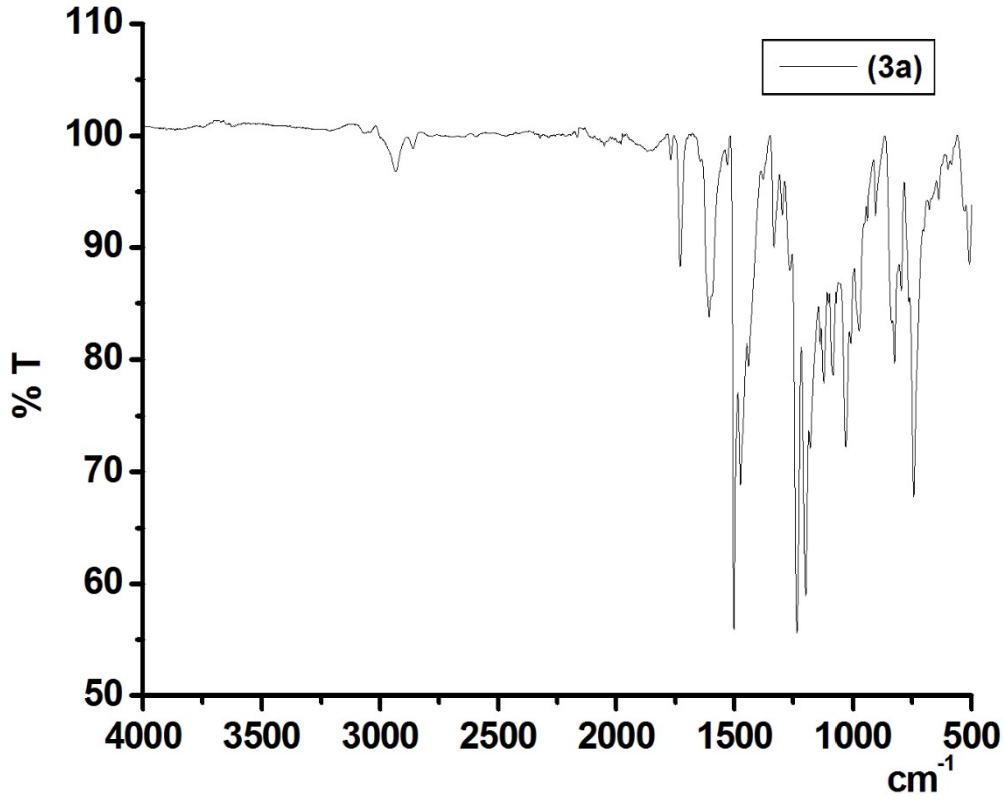

Fig. S3. FT-IR spectrum of the phthalocyanine **(3a)**

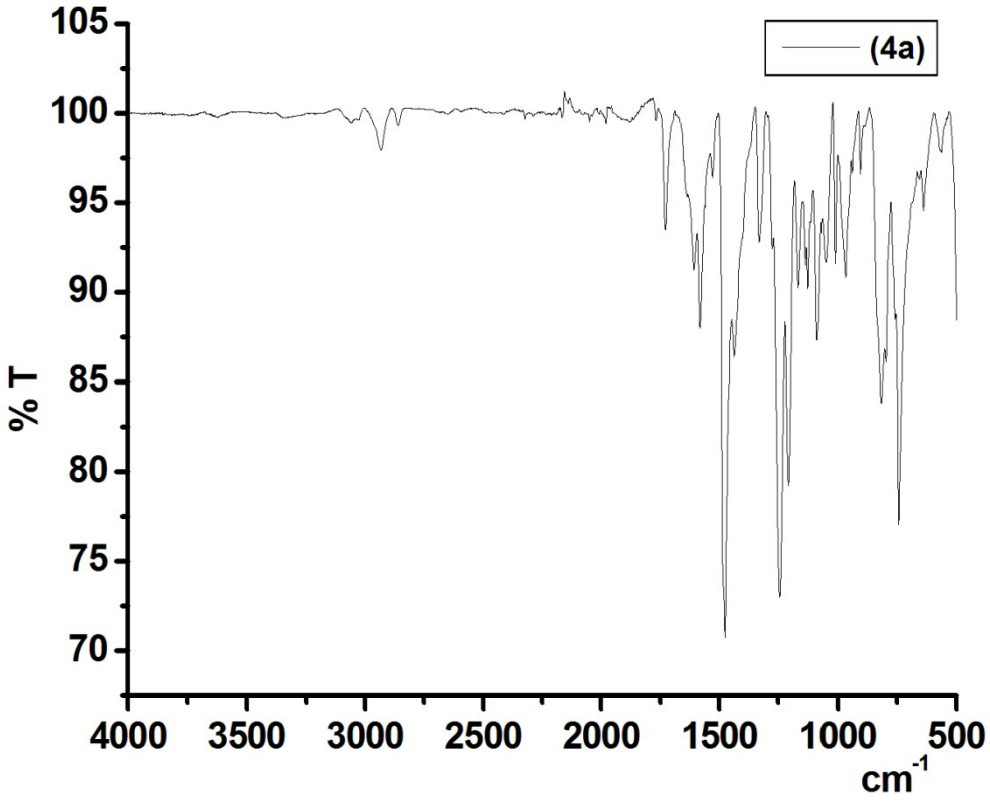

Fig. S4. FT-IR spectrum of the phthalocyanine **(4a)**

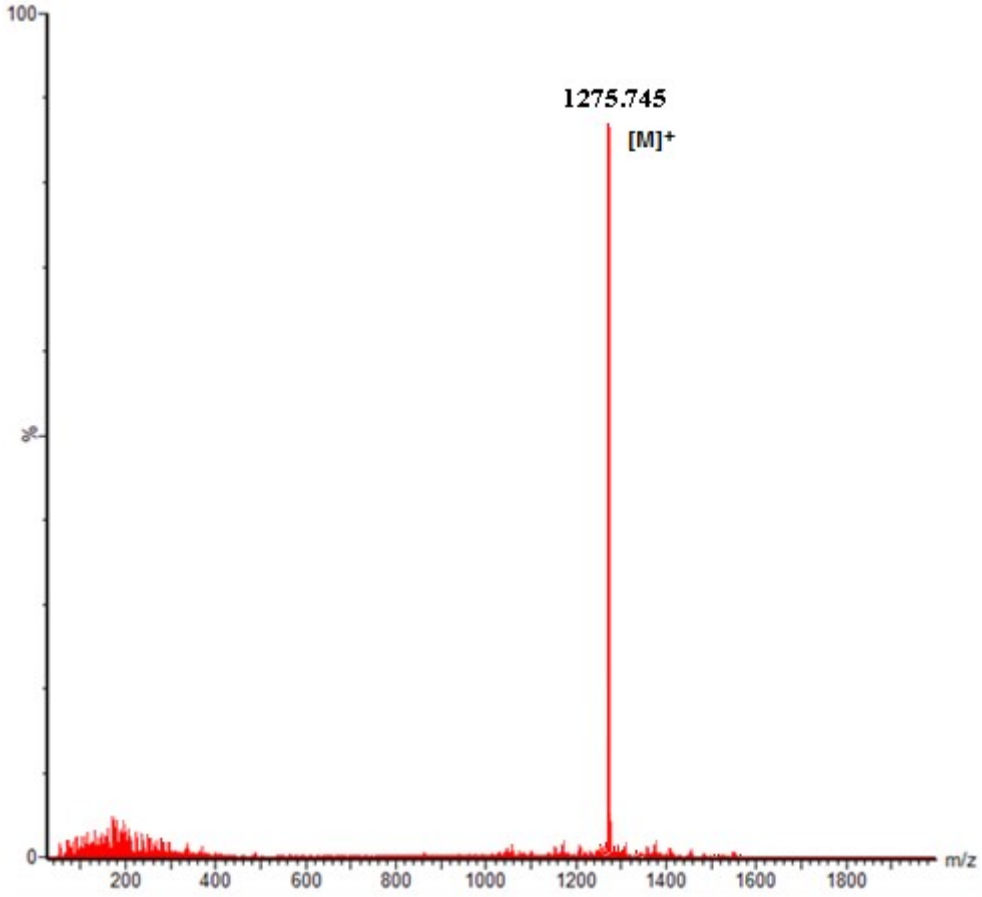

Fig. S5. MALDI TOF MS spectrum of the phthalocyanine **(1a)**

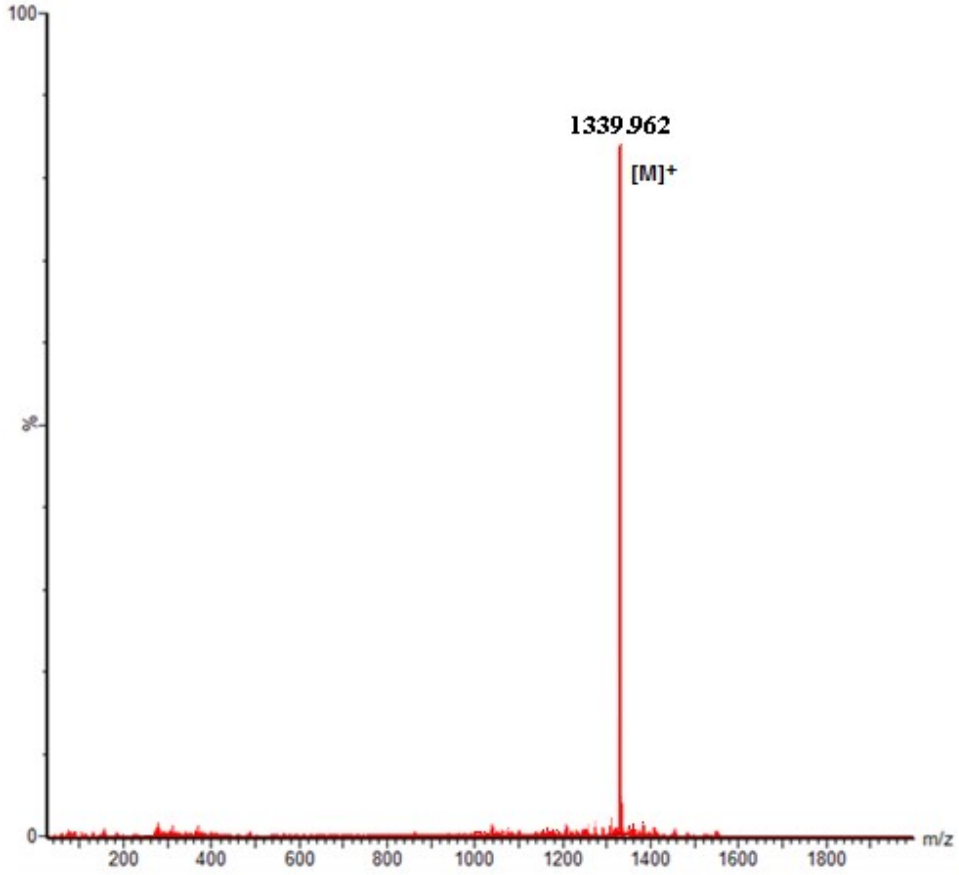

Fig. S6. MALDI TOF MS spectrum of the phthalocyanine **(2a)**

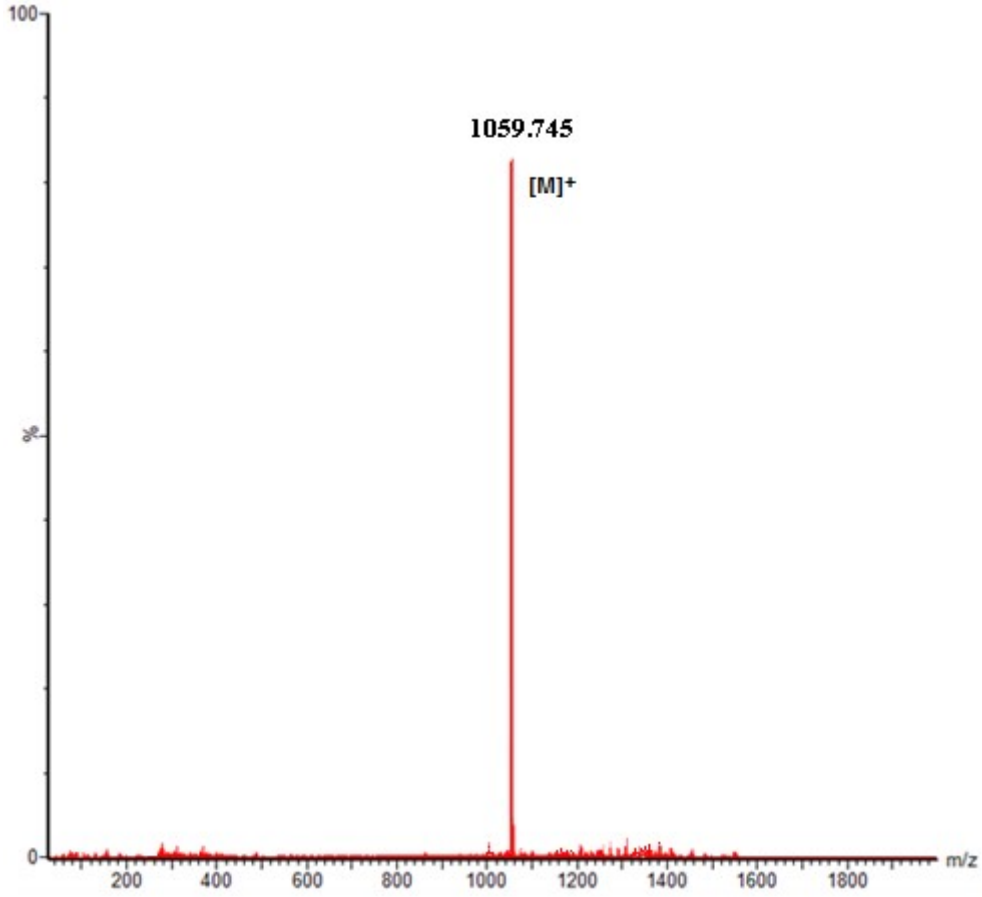

Fig. S7. MALDI TOF MS spectrum of the phthalocyanine **(3a)**

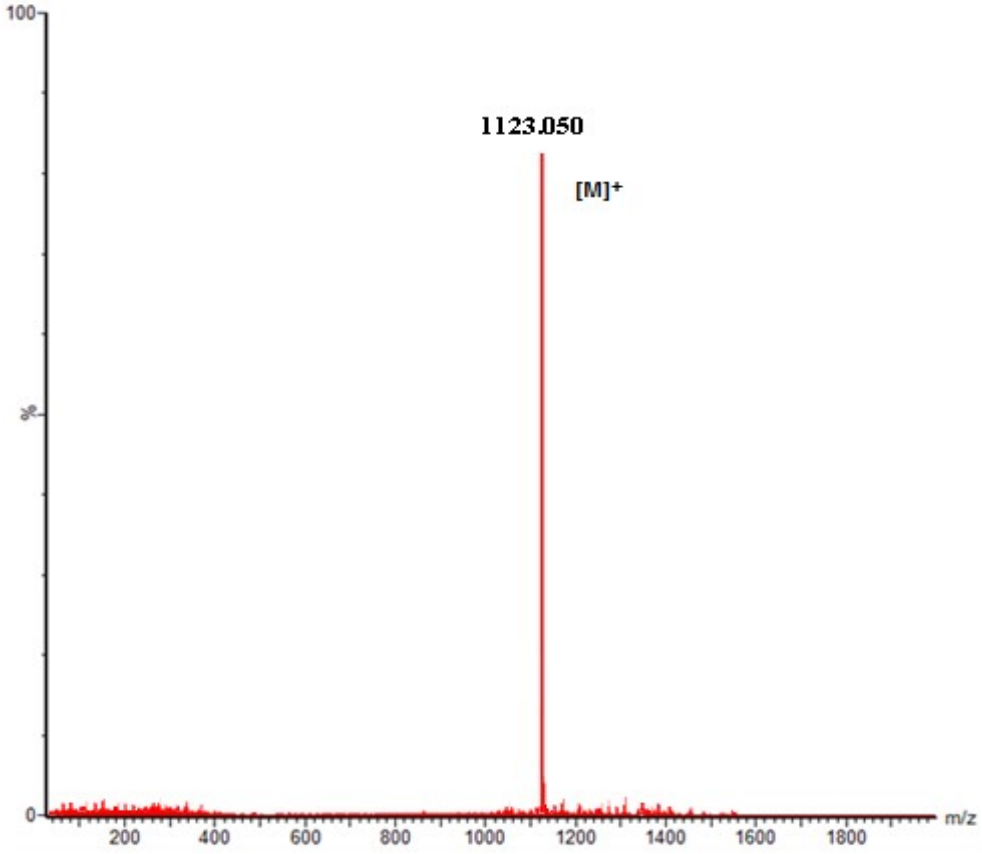

Fig. S8. MALDI TOF MS spectrum of the phthalocyanine **(4a)**

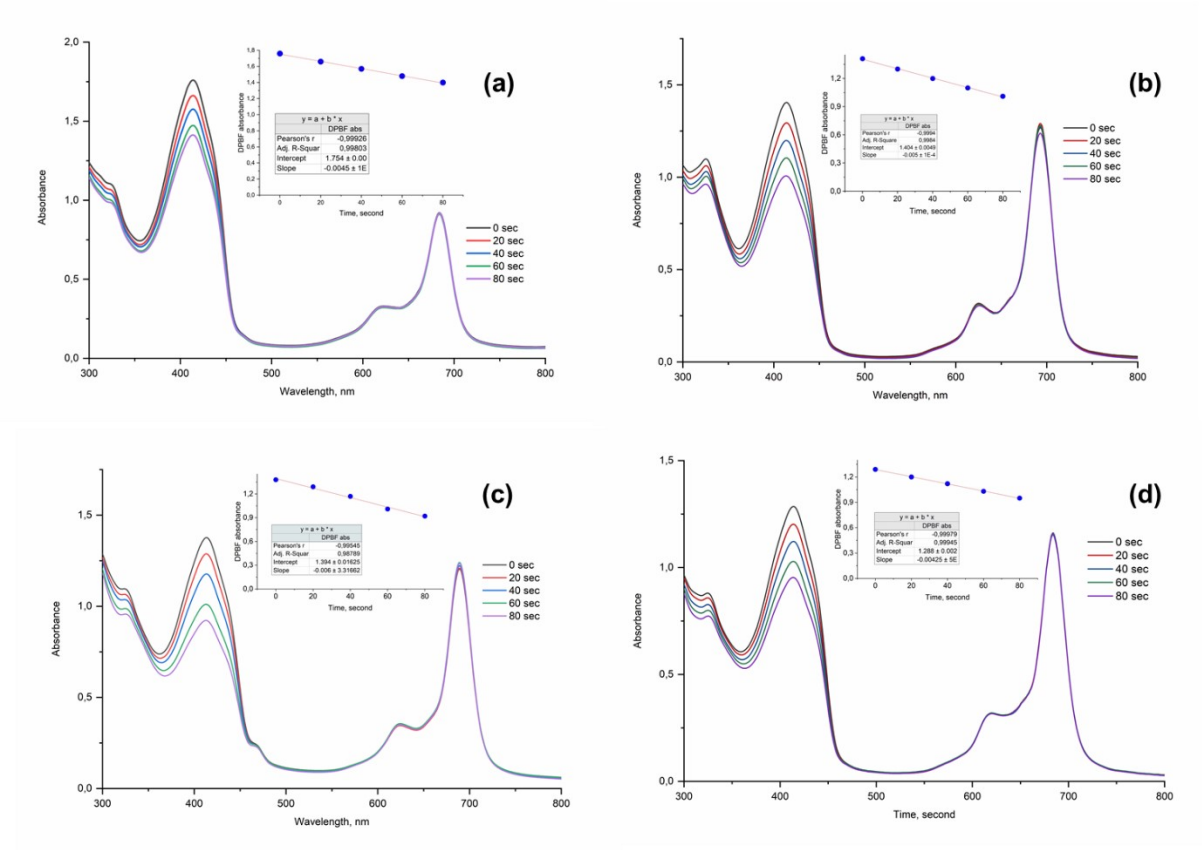

Fig. S9. UV-Vis electronic absorption changes during the determination of singlet oxygen quantum yield for non-peripheral tetra-substituted NiPc's [a) **(1a)**, b) **(3a)**, c) **(4a)**, and d) **(2a)**] in DMF.

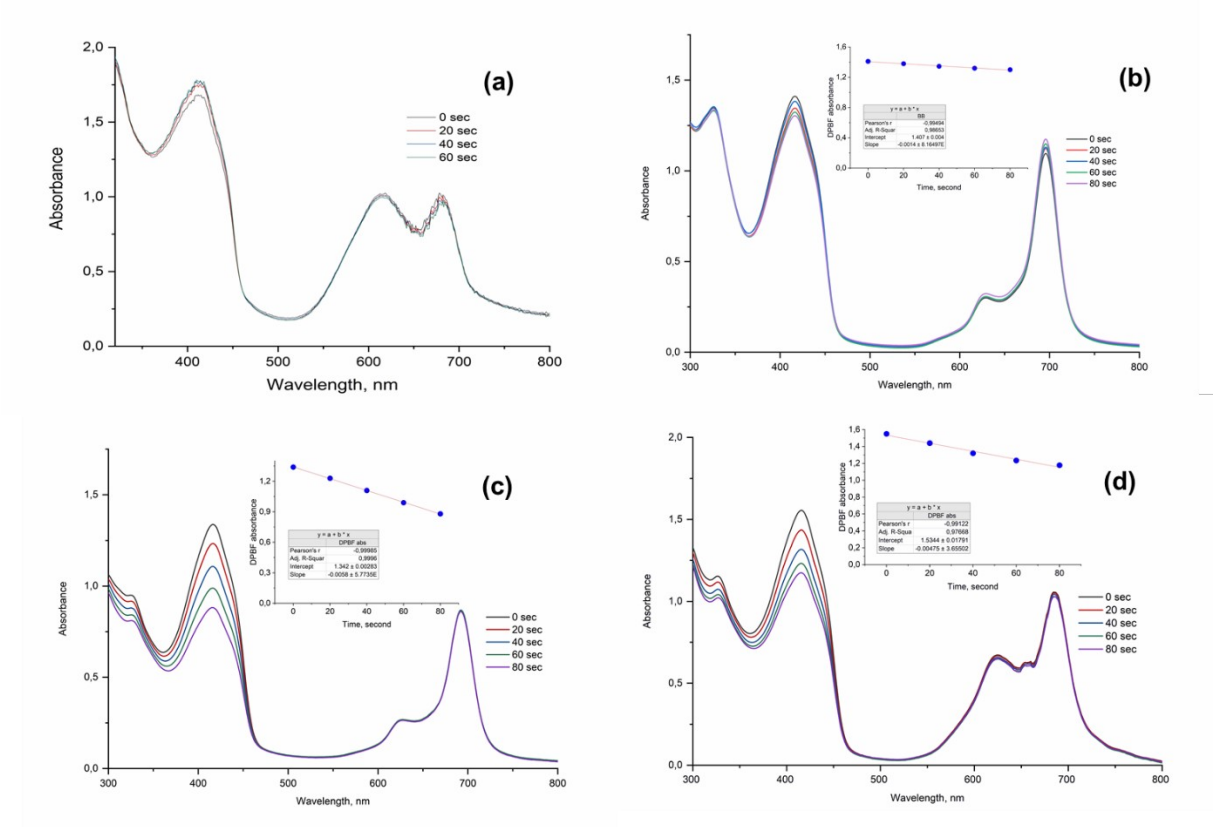

Fig. S10. UV-Vis electronic absorption changes during the determination of singlet oxygen quantum yield for non-peripheral tetra-substituted NiPc's [a) **(1a)**, b) **(3a)**, c) **(4a)**, and d) **(2a)**] in DMSO.

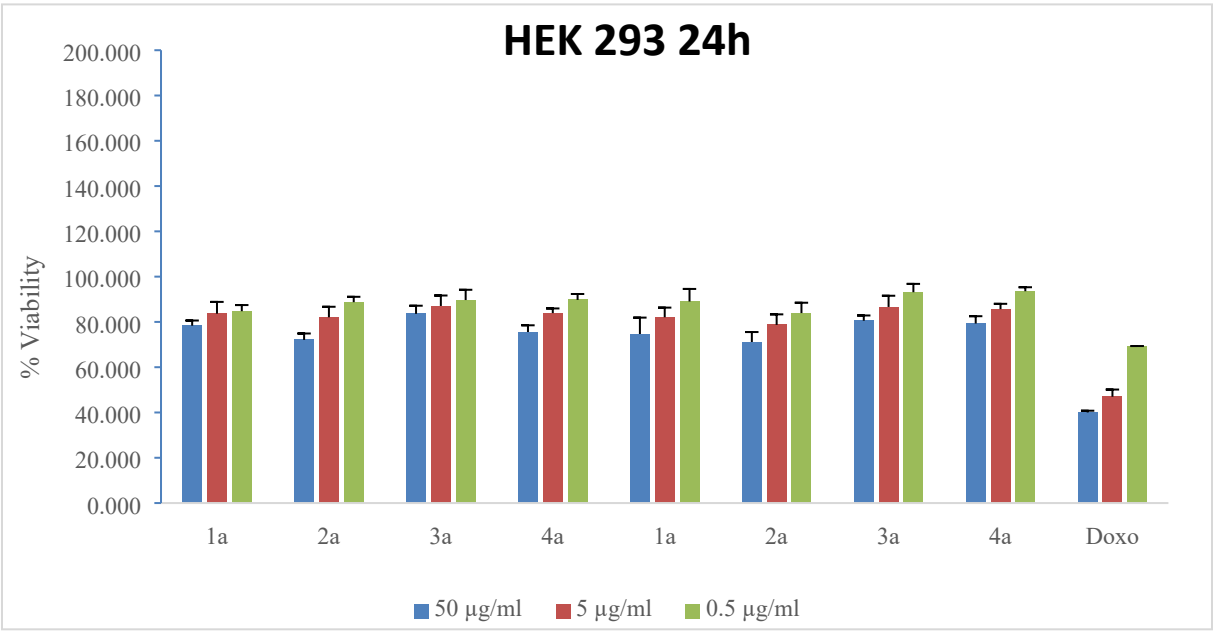

Fig. S11. Effects of different concentrations of compounds on RAW 293 cells viability determined by the MTT assay for 24 hours.

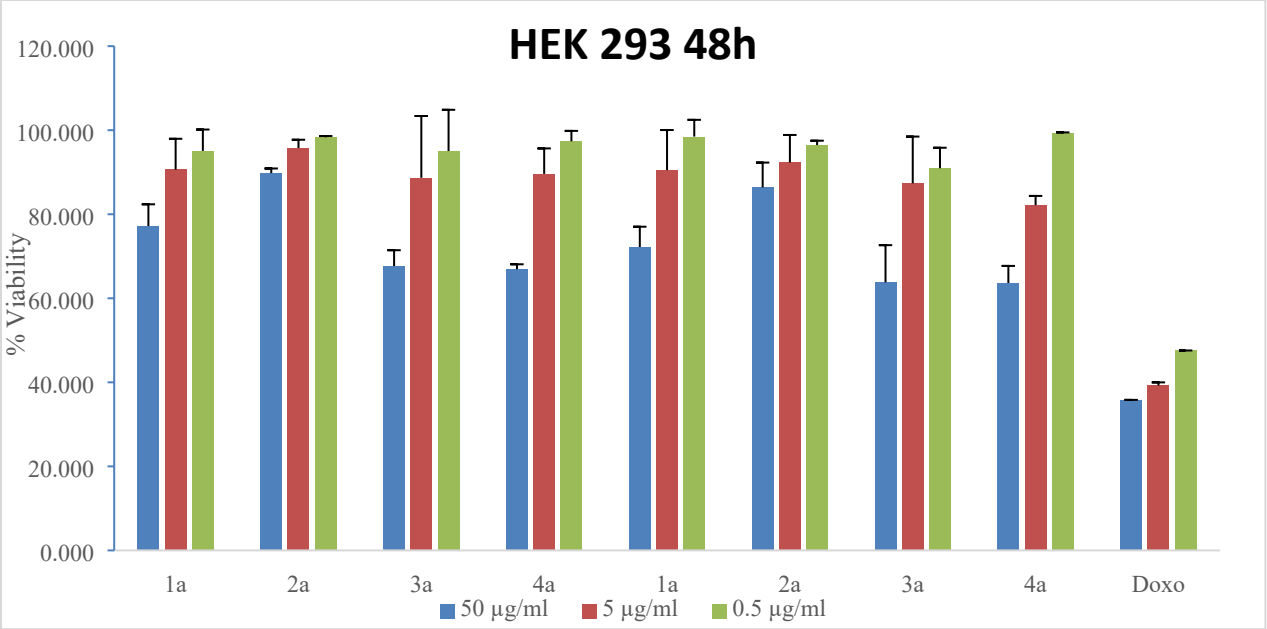

Fig. S12. Effects of different concentrations of compounds on RAW 293 cells viability determined by the MTT assay for 48 hours.

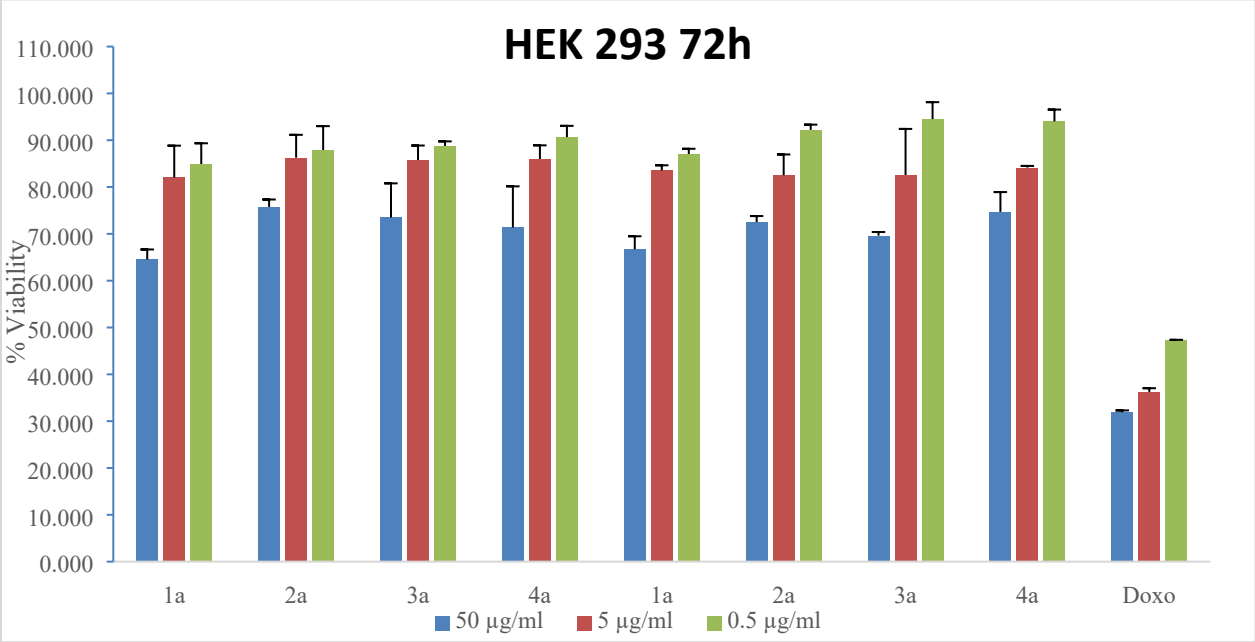

Fig. S13. Effects of different concentrations of compounds on RAW 293 cells viability determined by the MTT assay for 72 hours.

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