

New generation graphene-based dendritic phthalocyanine: Potential usage for biomedical applications

Yeni üretim grafen-tabanlı dendritik ftalosiyanın: Biyomedikal uygulamalar için potansiyel kullanımı

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SUMMARY

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Objective: It is aimed to produce new graphene-based materials with potential used in biomedical applications.

Method: The new GO-ZnPc hybrid was obtained by self-assembly method. Sonication was performed in the formation of hybrid. UV-Vis, emission spectra and scanning electron microscopy (SEM) were used to characterize ZnPc-GO hybrid formation.

Results: The GO solutions of different concentrations (0.0005 µg / mL; 0.005 µg / mL; 0.05 µg / mL; 0.4 µg / mL; 0.7 µg / mL; 1 µg / mL) prepared by sonication were added to 10 µg / mL ZnPc solution separately and sonicated again. UV-Vis, emission spectra and scanning electron microscopy (SEM) were used to characterize ZnPc-GO hybrid formation. All measurements showed that intermolecular interactions occurred after mixing the two components together, and the resulting hybrid was stable.

Conclusions: In this study, the new ZnPc-GO hybrid prepared and characterized. ZnPc and GO derivative was observed to well-coordinated. The obtained hybrid system was observed to have very interesting spectroscopic properties. It was observed that the GO-based ZnPc hybrid gave an absorption peak at 716 nm in the UV-Vis spectrum. The redshift observed with the ZnPc-GO hybrid formation in the UV spectra indicates that this material has the potential to be used in many biomedical applications, especially in tissue engineering and photodynamic therapy.

Keywords: Graphene oxide, phthalocyanine, dendrimer, biomedical applications

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ÖZET

Amaç: Biyomedikal uygulamalarda kullanılan potansiyele sahip yeni grafen bazlı materyallerin üretilmesi amaçlanmaktadır.

Yöntem: Yeni GO-ZnPc hibridi self-assembly yöntemiyle elde edildi. Sonikasyon işlemi hibrit oluşumunda kullanıldı. ZnPc-GO hibrid oluşumunu karakterize etmek için UV-Vis, emisyon spektrumları ve taramalı elektron mikroskopisi (SEM) kullanılmıştır.

Bulgular: Sonikasyonla hazırlanan farklı konsantrasyonlardaki (0.0005 µg / mL; 0.005 µg / mL; 0.05 µg / mL; 0.4 µg / mL; 0.7 µg / mL; 1 µg / mL) GO çözeltileri 10 µg / mL derişimindeki ZnPc çözeltisine ayrı ayrı eklendi ve tekrar sonikasyon yapıldı. ZnPc-GO hibrid oluşumunu karakterize etmek için UV-Vis, emisyon spektrumları ve taramalı

elektron mikroskopisi (SEM) kullanılmıştır. Tüm ölçümler, moleküller arası etkileşimlerin iki bileşenin birlikte karıştırılmasından sonra gerçekleştiğini ve sonuçta ortaya çıkan hibridin kararlı olduğunu gösterdi.

Sonuç: Bu çalışmada yeni ZnPc-GO hibrid hazırlandı ve karakterize edildi. ZnPc ve GO türevinin iyi koordine olduğu gözlemlendi. Elde edilen hibrit sistemin çok ilginç spektroskopik özelliklere sahip olduğu gözlemlendi. GO-bazlı ZnPc hibridin UV-Vis spektrumunda 716 nm'de absorpsiyon piki verdiği gözlemlendi. UV spektrumunda ZnPc-GO hibrid formasyonu ile gözlemlenen kırmızı kayma, bu malzemenin, özellikle doku mühendisliği ve fotodinamik terapide, birçok biyomedikal uygulamada kullanıma potansiyeline sahip olduğunu göstermektedir.

Anahtar sözcükler: Grafen oksit, ftalosiyanın, dendrimer, biyomedikal uygulamalar

INTRODUCTION

Graphene is nanomaterial that a single layer, 2-dimensional structure. Graphene and graphene derivatives have a high surface area, excellent electrical conductivity, strong mechanical strength, unparalleled thermal conductivity and remarkable biocompatibility¹. Graphene-based materials have the ability to adsorb various aromatic biomolecules through π - π stacking interaction and/or electrostatic interaction, making these compounds ideal materials for the fields of biosensors, drug delivery systems, and drug active substances. On the other hand, the hydrophobic nature of graphene prevents its use in the biomedical field. Graphene derivatives such as graphene oxide (GO) and reduced graphene oxide (RGO) have been extensively studied for various biomedical applications. GO with multiple oxygen-containing groups on graphene can be easily replaced with targeting ligands to facilitate targeted imaging and drug delivery^{1,2}. GO-based materials have the potential to be used in pharmaceutical carrier systems, biosensor applications, photodynamic therapy and bio-imaging². According to the literature, the use of GO-based materials is frequently seen in cancer treatment and photodynamic therapy applications³⁻¹⁰. Phthalocyanines have the potential to be used in many areas of advanced technology due to their interesting physical, chemical properties and stability. Phthalocyanines have also potential to be used especially in photodynamic therapy. There are many studies in the literature regarding the potential of phthalocyanine species to be used in the fields of photodynamic therapy^{11,12} and different biomedical areas¹³⁻¹⁵. The superior properties of phthalocyanines, especially red-

shifted Q bands in the UV spectrum, provide the potential for use in photodynamic therapy and photodynamic diagnosis¹³. Dendrimers are regularly branched structures with three-dimensional architecture. These structures with functional components located on the outer surface have interesting physical and chemical behavior and have the potential to be used in biomedical fields^{13,16-19}. It is expected that the new materials to be obtained by combining these species, which are highly active in medical applications, will have more interesting properties.

MATERIAL AND METHODS

The dendritic zinc(II) phthalocyanine (ZnPc) was prepared according to the literature (Figure 1)²⁰. DMSO, used as a solvent, is of spectroscopic purity. UV-vis spectra were recorded on a Shimadzu UV-1800 UV-vis spectrophotometer. An Agilent/Cary Eclipse G9800A fluorescence spectrophotometer was used for spectrofluorometric measurements. SEM images were taken at Tescan MIRA3 XMU. SONICS Vibra-Cell CVX750 sonicator was used for sonication. Graphene oxide and graphene oxide-phthalocyanine hybrid solutions were prepared at 700 Watt in sonicator.

Synthesis of graphene oxide-dendritic zinc(II) phthalocyanine hybrid

GO solutions at different concentrations (0.0005 $\mu\text{g} / \text{mL}$; 0.005 $\mu\text{g} / \text{mL}$; 0.05 $\mu\text{g} / \text{mL}$; 0.4 $\mu\text{g} / \text{mL}$; 0.7 $\mu\text{g} / \text{mL}$; 1 $\mu\text{g} / \text{mL}$) were prepared in DMSO by sonication. The solution of 10 $\mu\text{g} / \text{mL}$ of phthalocyanine in DMSO was added to these solutions, respectively. The prepared solutions were sonicated for 10 minutes.

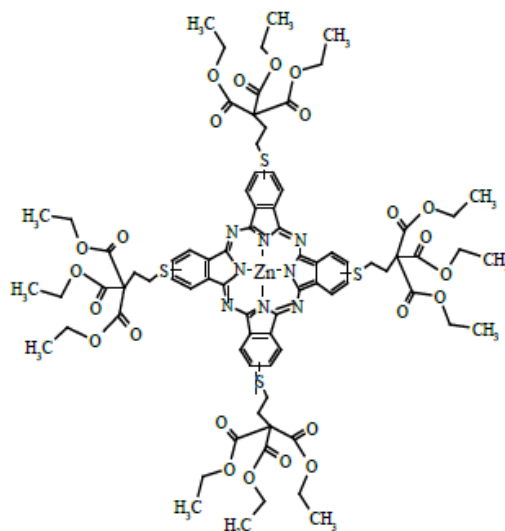


Figure 1: Molecular structure of ZnPc²⁰.

RESULTS

UV-Vis, emission spectra and scanning electron microscopy (SEM) were used to characterize ZnPc-GO hybrid formation.

The GO solutions of different concentrations (0.0005 $\mu\text{g} / \text{mL}$; 0.005 $\mu\text{g} / \text{mL}$; 0.05 $\mu\text{g} / \text{mL}$; 0.4

$\mu\text{g} / \text{mL}$; 0.7 $\mu\text{g} / \text{mL}$; 1 $\mu\text{g} / \text{mL}$) prepared by sonication were added to 10 $\mu\text{g} / \text{mL}$ ZnPc solution separately and sonicated again. The color changes of GO-ZnPc hybrids at different concentrations are shown in Figure 2. As can be seen from Figure 1, the color of the solutions changes significantly with the change in GO concentration.



Figure 2: The color change of ZnPc-GO hybrids at different concentrations (GO concentration increases from left to right).

UV-Vis spectra were examined after the interaction of GO solutions of different concentrations with ZnPc. ZnPc-GO hybrid formation was observed in the UV spectra by the changes in the characteristic Q-band for phthalocyanines. As shown in Figure 3, it was observed that binding was completed by the interaction of ZnPc at 10 $\mu\text{g} / \text{mL}$ and GO at 1 $\mu\text{g} / \text{mL}$. In the UV-Vis spectra, the addition of GO at different concentrations on ZnPc showed that the peaks gradually became flattened and a new peak formed. In addition, a redshift of 28 nm was observed in the spectrum. This shift is a significant value. It is seen that ZnPc and GO species are well-coordinated, especially π - π interactions due to conjugated structures.

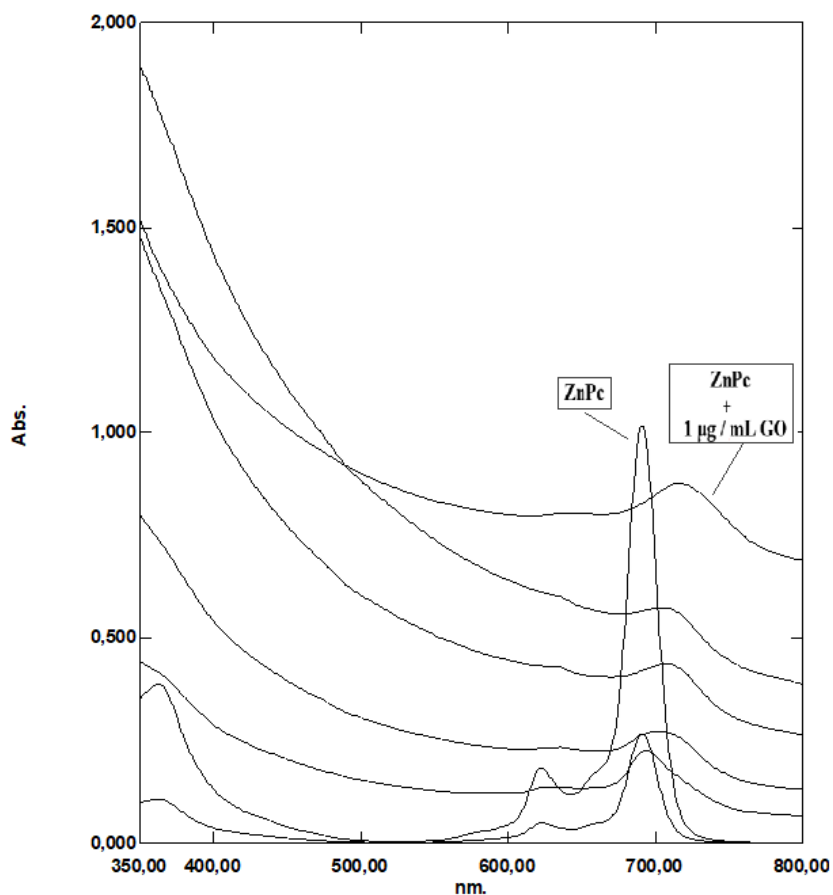


Figure 3: UV-Vis spectra depending on graphene oxide of different concentrations of ZnPc-GO hybrid (GO concentrations: 0.0005 $\mu\text{g} / \text{mL}$; 0.005 $\mu\text{g} / \text{mL}$; 0.05 $\mu\text{g} / \text{mL}$; 0.4 $\mu\text{g} / \text{mL}$; 0.7 $\mu\text{g} / \text{mL}$; 1 $\mu\text{g} / \text{mL}$).

Emission spectra were examined after the interaction of GO solutions of different concentrations with ZnPc for ZnPc-GO hybrid formation. As shown in Figure 4, it was observed that binding was completed by the interaction of ZnPc at 10 $\mu\text{g} / \text{mL}$ and GO at 1 $\mu\text{g} / \text{mL}$. Significant changes in peaks were observed with

the addition of GO at different concentrations on ZnPc in the emission spectra. These changes support the formation of the ZnPc-GO hybrid structure. It is observed that the formation of the ZnPc-GO hybrid significantly decreases in the area below the ZnPc emission peak.

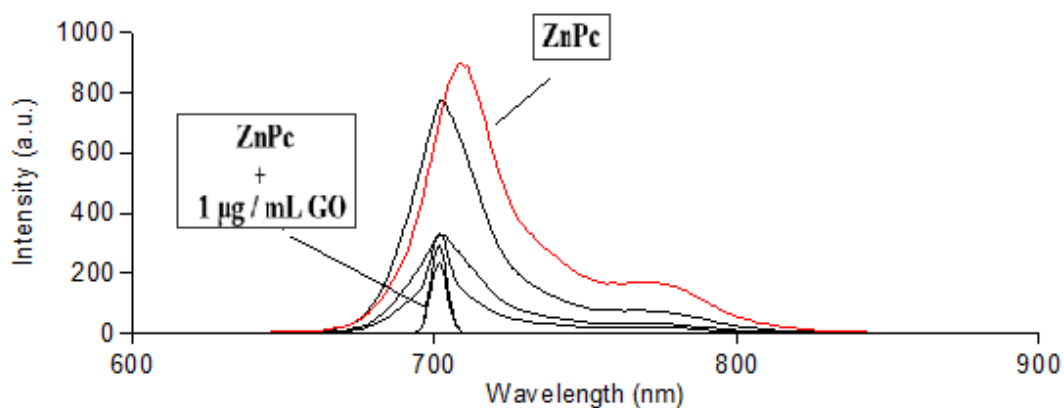


Figure 4: Emission spectra depending on graphene oxide of different concentrations of ZnPc-GO hybrid (GO concentrations: 0.0005 $\mu\text{g} / \text{mL}$; 0.005 $\mu\text{g} / \text{mL}$; 0.05 $\mu\text{g} / \text{mL}$; 0.4 $\mu\text{g} / \text{mL}$; 1 $\mu\text{g} / \text{mL}$)

The effect of sonication time on hybrid formation was also investigated. $0.4 \mu\text{g} / \text{mL}$ GO solutions were separately added to the ZnPc solutions and sonicated for 1, 5 and 10 minutes. UV-Vis and emission spectra of these solutions were examined. As shown in Figure 5, the ZnPc-GO hybrid

formation was observed to be complete in 10 minutes. The sonication time for the new ZnPc-GO hybrid was optimized to 10 minutes. Sonication time also has a significant effect on hybrid formation.

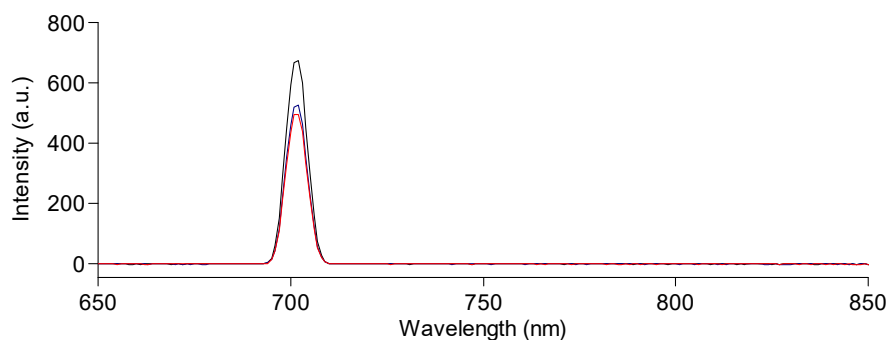


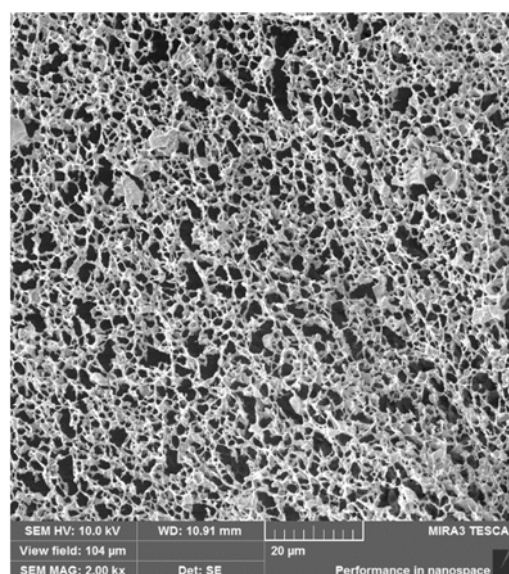
Figure 5: Emission spectra depending on sonication time of ZnPc-GO hybrid (1.min 5.min 10.min, (from top to bottom, respectively))

It is also seen from the SEM images that the binding of ZnPc increases as the concentration of GO increases (Figure 6). Figure 6 shows concentrations of GO in ZnPc as $0.005 \mu\text{g}/\text{mL}$ and $1 \mu\text{g}/\text{mL}$ GO. Increasing GO concentration increases the bridge formation and GO interlayer filling by ZnPc. The polymer chain branching

contiguity is obtained by increased concentration of GO by layered structure. The concentration of GO was adjusted to $1 \mu\text{g}/\text{mL}$ in ZnPc solution in DMSO and the structure is seen as GO of few-layer structures and combined to each other by increased concentration.



ZnPc + $0,0005 \mu\text{g}/\text{mL}$ GO



ZnPc + $1 \mu\text{g}/\text{mL}$ GO

Figure 6: SEM images of ZnPc-GO hybrids

DISCUSSION

The new GO-ZnPc hybrid was obtained by self-assembly method. Sonication was performed in the formation of hybrid. The effect of dilution on hybrid formation was investigated by absorption and fluorescence spectra. The effect of sonication on hybrid formation was also investigated by absorption and emission spectra. The sonication time also contributed to the formation of ZnPc-GO hybrid system. The formation of the obtained hybrids was also characterized by scanning electron microscopy (SEM).

By the formation of the ZnPc-GO hybrid, a redshift of 28 nm from the characteristic Q-band of ZnPc was observed in the UV spectrum. This change in the UV spectrum indicates that the ZnPc and GO species are well coordinated. The absorption of ZnPc-GO hybrid materials increases the potential of being used in many biomedical applications. The interaction between ZnPc and GO is thought to be π - π interactions due to its conjugated structures.

Significant changes were observed in the emission spectrum of the ZnPc-GO hybrid. The emission spectra also confirm the formation of the structure.

In the SEM images of the ZnPc-GO hybrid at different concentrations, it is observed that binding increases with increasing GO concentration. The SEM image on the right in figure 6 represents the fiber-like formation of GO-ZnPc composites. This composite formation can be a good candidate for both tissue engineering and UV sensitive polymers. Furthermore, the ZnPc-GO hybrid has the potential to be used as targeted drug delivery systems in photodynamic therapy as described in the literature^{21,22}.

All measurements showed that intermolecular interactions occurred after mixing the two components together, and the resulting hybrid was stable.

CONCLUSION

In this study, the new ZnPc-GO hybrid prepared and characterized. ZnPc and GO derivative was observed to well-coordinated. The obtained hybrid system was observed to have very interesting spectroscopic properties. It was observed that the GO-based ZnPc hybrid gave an absorption peak at 716 nm in the UV-Vis spectrum. The redshift observed with the ZnPc-GO hybrid formation in the UV spectra indicates that this material has the potential to be used in many biomedical applications, especially in tissue engineering and photodynamic therapy.

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REFERENCES

1. Yang Y, Asiri A M, Tang Z, Du D, Lin Y. Graphene based materials for biomedical applications. *Mater Today* 2013; 16: 365-373.
2. Nanda S S, Papaefthymiou G C, Yi D K. Functionalization of Graphene Oxide and its Biomedical Applications. *Crit Rev Solid State* 2015; 40: 291-315.
3. Huang P, Xu C, Lin J, Wang C, Wang X, Zhang C, Zhou X, Guo S, Cui D. Folic Acid-conjugated Graphene Oxide loaded with Photosensitizers for Targeting Photodynamic Therapy. *Theranostics* 2011; 1: 240-250.
4. Li Y, Dong H, Li Y, Shi D. Graphene-based nanovehicles for photodynamic medical therapy. *Int J Nanomed* 2015; 10: 2451-2459.
5. Zhou L, Zhou L, Wei S, Ge X, Zhou J, Jiang H, Li F, Shen J. Combination of chemotherapy and photodynamic therapy using graphene oxide as drug delivery system. *J Photoch Photobio B* 2014; 135: 7-16.
6. Shen H, Zhang L, Liu M, Zhang Z. Biomedical Applications of Graphene. *Theranostics* 2012; 2: 283-294.
7. Youssef Z, Vanderesse R, Colombeau L, Baros F, Roques-Carmes T, Frochot C, Wahab H, Toufaily J, Hamieh T, Acherar S, Gazzali A M. The application of titanium dioxide, zinc oxide, fullerene, and graphene nanoparticles in photodynamic therapy. *Cancer Nano* 2017; 8: 1-62.
8. Tabisha T A, Zhanga S, Winyard P G. Developing the next generation of graphene-based platforms for cancer therapeutics: The potential role of reactive oxygen species. *Redox Biol* 2018; 15: 34-40.
9. Krajczewski J, Rucińska K, Townley H E, Kudelski A. Role of various nanoparticles in photodynamic therapy and detection methods of singlet oxygen. *Photodiag Photodyn Therapy* 2019; 26: 162-178.
10. Nene L C, Managa M, Nyokong T. Photo-physicochemical properties and in vitro photodynamic therapy activity of morpholine-substituted Zinc(II)-Phthalocyanines π - π stacked on biotinylated graphene quantum dots. *Dyes Pigments* 2019; 165: 488-498.

11. Jinling H, Naisheng C, Jiandong H, Ersheng L, Jinping X, Suling Y, Ziqiang H, Jiancheng S. Metal phthalocyanine as photosensitizer for photodynamic therapy (PDT). *Sci In China (Series B)* 2001; 44: 113-122.
12. Lukyanets E A. Phthalocyanines as Photosensitizers in the Photodynamic Therapy of Cancer. *J Porph Phthalocya* 1999; 3: 424-432.
13. Figueiraa F, Pereiraa P M R, Silvaa S, Cavaleiroa J AS, Tomé J P C, Porphyrins and Phthalocyanines Decorated with Dendrimers: Synthesis and Biomedical Applications. *Curr Org Synth* 2014; 11: 110-126.
14. Mody T D. Pharmaceutical development and medical applications of porphyrin-type macrocycles. *J Porph Phthalocya* 2000; 4: 362-367.
15. Li X, Zheng B D, Peng X H, Li S Z, Ying J W, Zhao Y, Huang J D, Yoon J. Phthalocyanines as medicinal photosensitizers: Developments in the last five years. *Coord. Chem. Rev* 2019; 379: 147-160.
16. Boas U, Heegaard P M H. Dendrimers in drug research. *Chem Soc Rev* 2004, 33(1), 43-63.
17. Medina S H, El-Sayed M E H. Dendrimers as carriers for delivery of chemotherapeutic agents. *Chem Rev* 2009; 109(7): 3141-3157.
18. Tekade R K, Kumar P V, Jain N K. Dendrimers in oncology: an expanding horizon. *Chem Rev* 2010; 110(4): 2574-2574.
19. Jeong Y H, Yoon H J, Jang W D. Dendrimer porphyrin-based self-assembled nano-devices for biomedical applications. *Polymer J* 2012; 44: 512-521.
20. Yabaş E, Sülü M, Özgür A, Tutar Y. Effect of New Water-Soluble Dendritic Phthalocyanines on Human Colorectal and Liver Cancer Cell Lines. *Süleyman Demirel University J Natur Appl Sci* 2017; 21: 689-695.
21. Zhou L, Zhou L, Wei S, Ge X, Zhou J, Jiang H, Li F, Shen J. Combination of chemotherapy and photodynamic therapy using graphene oxide as drug delivery system. *J Photochem Photobiol B* 2014; 135: 7-16.
22. Huang P, Xu C, Lin J, Wang C, Wang X, Zhang C, Zhou X, Guo S, Cui D. Folic Acid-conjugated Graphene Oxide loaded with Photosensitizers for Targeting Photodynamic Therapy. *Theranostics* 2011; 1: 240-250.