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

Ebru Yabaş

Sivas Cumhuriyet University, Advanced Technology Research and Application Center, Sivas, Turkey
Corresponding author: Ebru Yabaş, Sivas Cumhuriyet University, Advanced Technology Research and Application Center, Sivas, Turkey
E-mail: eyabas@cumhuriyet.edu.tr
Received/Accepted: July 23, 2019 /September 30, 2019
Conflict of interest: There is not a conflict of interest.

SUMMARY

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

ÖZET

Amaç: Biyomedikal uygulamalarla 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: Sonikasyonda 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 kullanılmıştır. ZnPc-GO hibridinin oluşumunu karakterize etmek için UV-Vis, emisyon spektrumları ve taramalı elektron mikroskopisi kullanılmıştır.
elektron mikroskopisi (SEM) kullanılmıştır. Tüm ölçümler, moleküler arası etkileşimlerin iki bileşenin birlikte
karsıtıldığını sonra gerçekleştiği ve sonucu ortaya çıkan hibridin karartılı olduğunu gösterdi.
Sonuç: Bu çalışmada yeni ZnPc-GO hibrid hazırlanı ve karakterize edildi. ZnPc ve GO türevinin iyi koordinde olduğu
özüntü. Elde edilen hibrit sistemden çok ilginç spektroskopik özellikler sahip olduğunu gözlemledi. 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 malzemeden, özellikle doku mühendisliği ve fotodinamik terapide, birçok biyomedikal
uygulamada potansiyeline sahip olduğunu göstermektedir.
Anahtar sözcükler: Grafen oksit, ftalosiyanin, 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
bio-compatibility. 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. GO-based materials have the
potential to be used in pharmaceutical carrier
systems, biosensor applications, photodynamic
therapy and bio-imaging. According to the
literature, the use of GO-based materials is
frequently seen in cancer treatment and
photodynamic therapy applications. 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 and
different biomedical areas. The superior
properties of phthalocyanines, especially
shifted Q bands in the UV spectrum, provide the
potential for use in photodynamic therapy and
photodynamic diagnosis. 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. 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). 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 MIRA 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
µg / mL; 0.005 µg / mL; 0.05 µg / mL; 0.4 µg / mL;
0.7 µg / mL; 1 µg / mL) were prepared in DMSO
by sonication. The solution of 10 µg / mL of
phthalocyanine in DMSO was added to these
solutions, respectively. The prepared solutions
were sonicated for 10 minutes.
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 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. 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.

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 µg / mL and GO at 1 µg / 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 µg / mL; 0.005 µg / mL; 0.05 µg / mL; 0.4 µg / mL; 0.7 µg / mL; 1 µg / 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 µg / mL and GO at 1 µg / 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 µg / mL; 0.005 µg / mL; 0.05 µg / mL; 0.4 µg / mL; 0.7 µg / mL; 1 µg / mL)
The effect of sonication time on hybrid formation was also investigated. 0.4 µg/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 µg/mL and 1 µg/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 µg/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.

**Figure 6:** SEM images of ZnPc-GO hybrids

ZnPc + 0.0005 µg/mL GO  
ZnPc + 1 µg/mL GO
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.

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.

Acknowledgments

In this study, the laboratory facilities of the Advanced Technology Application and Research Center (CÜTAM) of Sivas Cumhuriyet University were used.

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, Frochet 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, Zhang 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.

Acknowledgments

In this study, the laboratory facilities of the Advanced Technology Application and Research Center (CÜTAM) of Sivas Cumhuriyet University were used.

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, Frochet 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, Zhang 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, Porphyrs 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, Özugür 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.