Academic Research Journal of Technical Vocational Schools

| artes@cumhuriyet.edu.tr | Founded: 2023 Available online, ISSN: 2822-5880 Publisher: Sivas Cumhuriyet Üniversitesi

Antioxidant Activity of Oxadiazole-Tetrasubstituted Magnesium Phthalocyanine Compound

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ResearchArticle

History

Received: 02/12/2022
Accepted: 24/03/2023

ABSTRACT

This study is a study examining the antioxidant activity of oxadiazole tetrasubstituted magnesium phthalocyanine compound. In vitro antioxidant activities such as 2,2-diphenyl-1picrylhydrazil (DPPH) radical scavenging activities, total phenolic and flavonoid contents of the phthalocyanine compound obtained as a result of the tetramerization reaction of oxadiazole substituted phthalonitrile derivative were investigated. It was found that the compound reacted significantly with DPPH as well as a high total phenol content. According to the obtained data, it can be said that the phthalocyanine compound, whose properties were examined, has antioxidant activity.

Keywords: Phthalocyanine, Antioxidant, DPPH, Total Phenolic Content, Total Flavonoid Content.

Oksadiazol-Tetrasübstitüye Magnezyum Ftalosiyanin Bileşiğinin Antioksidan Aktivitesi

Süreç

Geliş: 02/12/2022
Kabul: 24/03/2023

ÖZ

Bu çalışma oksadiazol tetrasübstitüe magnezyum ftalosiyanin bileşiğinin antioksidan aktivitesini inceleyen bir çalışmadır. Oksadiazol sübstitüe ftalonitril türevinin tetramerizasyon reaksiyonu sonucu elde edilen ftalosiyanin bileşiğinin 2,2-difenil-1pikrilhidrazil (DPPH) radikal yakalama aktiviteleri, toplam fenolik ve flavonoid içerikleri gibi in vitro antioksidan aktiviteleri araştırıldı. Bileşiğin, yüksek toplam fenol içeriğinin yanı sıra DPPH ile önemli ölçüde reaksiyona girdiği belirlendi. Elde edilen verilere göre özellikleri incelenen ftalosiyanin bileşiğinin antioksidan aktiviteye sahip olduğu söylenebilir.

Anahtar Kelimeler: Ftalosiyanin, Antioksidan, DPPH, Toplam Fenolik İçeriği, Toplam Flavonoid İçeriği.

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How to Cite: Yabaş E., Uçar Sözmen E., (2023) Antioxidant Activity of Oxadiazole-Tetrasubstituted Magnesium Phthalocyanine Compound, Academic Research Journal of Technical Vocational Schools, 2(1):1-4

Introduction

Reactive species are unstable substances that can be produced physiologically or as a result of certain pathological conditions such as inflammation, cancer, cardiovascular disease, and diabetes (Sharma et al., 2012; Apel et al., 2004; Lushchak, 2014; Özdemir et al., 2020; Ağırtaş et al., 2022). Antioxidants play an important role in preventing or slowing down cell damage caused by reactive species such as free radicals. Antioxidants can be obtained naturally or synthetically (Nimse et al., 2015; Eken-Korkut et al., 2021). In particular, the design and production of new substances that can be produced synthetically and show high activity are of great importance in applications.

It has been observed in the literature that phthalocyanine macrocycles have promising antioxidant potentials (Amaral et al., 2012; Söylemez et al., 2018). Phthalocyanines are known as biologically active macrocyclic compounds with stable 18-π electron system. In particular, they are preferred as photosensitive drugs in photodynamic therapy (PDT) applications, since they do not show toxic properties and have strong absorption between 600 and 800 nm (Yıldırım et al., 2017; Özdemir et al., 2020). The properties of these macromolecules can be changed depending on the type of substituents and metal centers to be attached to the phthalocyanine ring. In particular, the effectiveness and diversity of these compounds in the medical field can be increased. In addition, it is reported in the literature that the photodamaging effect of photosensitizers used in PDT increases due to the activities of some antioxidant species (Fatima et al., 2016; Günsel et al., 2019).

On the other hand, it is stated that oxadiazole and its derivatives show a wide range of biological activities including antioxidant agents and are in a class of compounds widely used in medicinal chemistry (Kotaiah et al., 2012; Gobec et al., 2015).

When evaluated in this context, it is thought that the type of compound obtained by combining two compound classes with the potential to be used in biological applications can show more effective properties.

For this purpose, we examined the antioxidant activity of the oxadiazole tetrasubstituted magnesium phthalocyanine compound, which we synthesized and showed potential anticancer activity, and observed that they showed antioxidant activity.

Material and methods

All chemicals used in the experiments were purchased from Merk. Water-soluble magnesium phthalocyanine was synthesized due to literature (Yabaş et al., 2022). The synthesis method is briefly summarized below.

Synthesis of Magnesium Phthalocyanine

1,8-Diazabicyclo [5.4.0] undec-7-ene (DBU) was added to the mixture of oxadiazole-substituted phthalonitrile compound and magnesium acetate tetrahydrate in dimethylformamide (DMF) under nitrogen gas and heated at 180°C for 20 hours. At the end of the reaction, the organic phase was precipitated with MeOH and filtered. The crude product was washed with water, MeOH, and acetone (using the soxhlet apparatus), respectively, and dried. The resulting product was characterized by 1H-NMR, UV-Vis, ATR-IR, MALDI-TOF MS and elemental analysis.

Antioxidant Activity

DPPH radical scavenging activity of the water-soluble magnesium phthalocyanine compound was evaluated according to the method of Blois (1958).

Total phenolic content (TPC) was determined by the spectrophotometric method (Clarke et al., 2013) and clarified as gallic acid equivalents.

Total flavonoid content (TFC) was determined by the aluminum chloride colorimetric method of Molan and Mahd (2014).

Results and Discussion

In this study, the antioxidant activity of oxadiazole substituted magnesium phthalocyanine compound, which is a compound obtained by combining oxadiazole and phthalocyanine compounds, which are biologically active compound classes, was investigated. According to the literature, oxadiazole substituted magnesium phthalocyanine compound was obtained as a result of tetramerization reaction in the presence of metal salt of oxadiazole substituted phthalonitrile. The obtained product was easily purified by washing with solvents by taking advantage of the solubility differences. The chemical structure of the purified oxadiazole-tetrasubstituted magnesium phthalocyanine compound was elucidated by characterization techniques such as 1H-NMR, UV-Vis, ATR-IR, MALDI-TOF MS and elemental analysis. Cytotoxic studies of the quaternized derivative of the oxadiazole-substituted magnesium phthalocyanine compound were also carried out by Yabaş et. al. (2022). In these studies, it was determined that this synthesized compound has a high potential to be used as an anti-cancer agent. When evaluated from this point of view, it is that the of the compound whose antioxidant properties were examined in this study may show high activity in biological applications.

In this study, whose chemical structure is shown in Figure 1, were investigated. Antioxidant activities were investigated in the solution medium obtained by dissolving the phthalocyanine compound in dimethyl sulfoxide (DMSO).

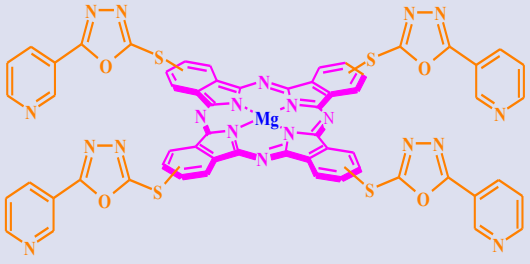

Figure 1. Chemical structure of oxadiazole tetrasubstituted magnesium phthalocyanine

Antioxidant activities were investigated in the solution medium obtained by dissolving the phthalocyanine compound in dimethyl sulfoxide (DMSO). The antioxidant activity of the compound was compared with the gallic acid standard studied under the same conditions. In the solution medium, a visible decrease in the distinctive purple color of DPPH was observed as a result of the formation of a reaction between the phthalocyanine compound and DPPH. In this case, we can say that DPPH is reduced by the phthalocyanine compound. However, in the experiments, a decrease in absorbance value was observed because precipitation occurred in the solutions in the 96-well plate and as a result, homogeneity could not be achieved in the solution during the measurement. As a result, it was determined that the antioxidant activity of the oxadiazole-substituted magnesium phthalocyanine compound was weaker than the gallic acid standard substance (Figure 2).

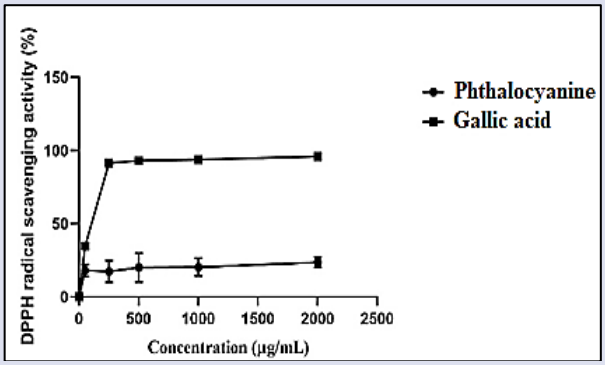

Figure 2. The *In vitro* DPPH Radical Scavenging Activity of oxadiazole-substituted magnesium phthalocyanine.

TPC and TFC properties of the compound were also investigated. As seen in Figure 3, according to the results obtained, it was seen that the total phenol content was high and the flavonoid content was very low.

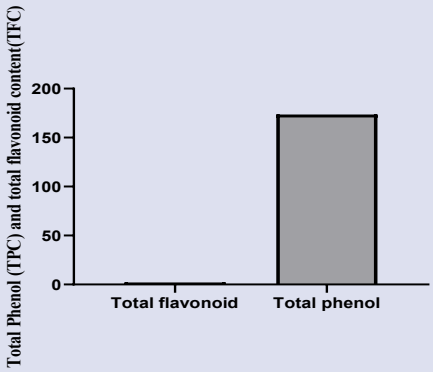

Figure 3. The *In vitro* TPC and TFC properties of oxadiazole-substituted magnesium phthalocyanine.

Conclusions

In this study, the antioxidant activity of oxadiazole tetrasubstituted magnesium phthalocyanine compound synthesized according to the literature was investigated. Oxadiazole and phthalocyanine compounds are in the class of important compounds with high biological activity. We planned such a study, thinking that the new compound group obtained by the combination of these two groups may exhibit more interesting activities.

In the related literature, a water-soluble quaternized derivative of the oxadiazole tetrasubstituted magnesium phthalocyanine compound we used in this study was synthesized. It was determined that this water-soluble compound selectively exhibited highly effective anti-cancer activity. Based on this goal, we investigated in vitro antioxidant activities such as DPPH radical scavenging activities, total phenolic and flavonoid contents of oxadiazole tetrasubstituted magnesium phthalocyanine compound. The compound was observed to react significantly with DPPH. In addition, the total phenol content, which is important in terms of antioxidant activity value, was found to be high. Looking at these data, it can be said that the investigated compound has antioxidant activity.

Conflicts of Interest

There are no conflicts to declare.

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