Research Article

ANTIOXIDANT, ANTIMICROBIAL ACTIVITY AND DNA PROTECTIVE EFFECT OF MESPILUS GERMANICA (L)

Elif GÜLBAHCE MUTLU[1], Hatice TANER SARAÇOGLU[2], Nursena ARSLAN[3], Emine ARSLAN[4], Gökhan ZENGİN[5]

Abstract

Aim: Medlar (*M. germanica*) is a durable plant which have hard fruits. In this study, it was aimed to determine the antioxidant, antimicrobial activity and DNA protective effects of both fruit and seed extracts of medlar.

Method: Antioxidant capacities of extracts of medlar was determined by using the DPPH method, Folin-Ciocaltaeu method was used for total phenolic content and the antimicrobial effect of the extract against 16 bacteria was investigated.

Findings: As a result of the study, the possible protective effect of medlar fruit extracts obtained at different concentrations against DNA damage was determined. In addition, it was revealed that the total phenolic contents and radical scavenging activities of the seed extracts were higher than the fruits extracts. While the medlar seed extract used in the study did not show any effect against bacteria, the fruit extract of this plant had various effects on the bacteria used. In addition, it was determined that the medlar fruit extract had a protective effect in DNA+UV, DNA+H_2O_2 and DNA+UV+$H2O_2$ applications.

Results: According to the results obtained, it was observed that *M. germanica* could provide protection against oxidative stress.

Keywords: Antimicrobial, DNA protective effect, Free radical scavenging, *Mespilus germanica*, Phenolic contents.

[1] Assistant Professor, KTO Karatay University, Faculty of Medicine, Department of Medical Biology, Karatay, Konya, Turkey, elif.mutlu@karatay.edu.tr ORCİD: 0000-0003-2391-2152
[2] Assistant Professor, Selçuk University, Faculty of Science, Department of Biology, Selçuklu, Konya, Turkey, htaner@selcuk.edu.tr, ORCİD: 0000-0001-9502-3739
[3] İstanbul Medipol University, Faculty of Dentistry Turkey, nursenaarslan26@gmail.com ORCİD: 0000-0002-8774-383X
[4] Corresponding Author: Professor, Selçuk University, Faculty of Science, Department of Biology, Selçuklu, Konya, Turkey, earslan@selcuk.edu.tr, ORCİD: 0000-0002-0782-506X
[5] Professor, Selçuk University, Faculty of Science, Department of Biology, Selçuklu, Konya, Turkey, gokhanzengin@selcuk.edu.tr, ORCİD: 0000-0001-6548-7823

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Mespilus germanica (L)nin Antioksidan, Antimikrobiyal Aktivitesi ve DNA Koruyucu Etkisi

Öz

Amaç: Muşmula (*M. germanica*) sert meyveleri olan dayanıklı bir bitkidir. Bu çalışmada muşmulanın hem meyve hem de tohum ekstraktının antioksidan, antimikrobiyal aktivitesi ve DNA koruyucu etkilerinin belirlenmesi amaçlanmıştır.

Yöntem: Muşmula ekstraktlarının antioksidan kapasitesi DPPH yöntemi kullanılarak belirlenmiş, toplam fenolik içerik için Folin-Ciocaltaeu yöntemi kullanılmış ve ayrıca ekstraktın 16 bakteriye karşı antimikrobiyal etkisi araştırılmıştır.

Bulgular: Çalışma sonucunda farklı konsantrasyonlarda elde edilen muşmula meyve ekstraktların DNA hasarına karşı olası koruyucu etkisi belirlendi. Bunun yanı sıra tohum ekstraktlarının toplam fenolik içeriklerinin ve radikal yakalama aktivitelerinin meyve ekstraktından daha yüksek olduğu ortaya çıktı. Çalışmada kullanılan muşmula tohum ekstraktını bakterilere karşı herhangi bir etki göstermez iken, bu bitkinin meyve ekstraktının kullanılan bakteriler üzerinde çeşitli etkileri oldu. Ayrıca, muşmula meyvesi ekstraktının DNA+UV, DNA+H_2O_2 ve DNA+UV+H_2O_2 uygulamalarında koruyucu etkiye sahip olduğu belirlendi.

Sonuç: Elde edilen sonuçlara göre, *M. germanica*'nın oksidatif strese karşı koruma sağlayabildiği gözlendi.

Anahtar Kelimeler: Antimikrobiyal, DNA koruyucu etki, Serbest radikal süpürücü, *Mespilus germanica*, Fenolik içerik.

1. INTRODUCTION

Medlar which belongs to the Rosaceae family grows cold and sore at dark places (Żołnierczyk et al., 2021). The fruits of medlar which is brown also sometimes -reddish tinged which are 1.5 to 3 cm in diameter and small ones have 10–80 g weight is harvested in the fall (Browicz et al., 1972; Bignami et al., 200; Gülçin et al., 2011). Medicinal plants have been used as treatment of certain diseases. These plants are used to drug treatment, which are more preferred because of less toxic and almost free from side effect (Davoodi et al., 2018). Fruits and leaves of medlar which also contain a various phytochemical such as phenolics and flavonoids are used as therapeutic purposes (Oktay et al., 2003; Bibalani et al., 2012). Plants phytochemical feature are very important because of they have antioxidant which obligatory to environmental acclimation and adaptation. So, recent studies are investigated that antioxidant properties of plants which are important for knowledge nutraceutical and pharmaceutical properties of these plant (Llauradó Maury et al., 2020). Free radicals are generated in human by pathological states, physiochemical conditions, or endogenous systems. A balance among free radicals and antioxidants is necessary to proper physiological functions and antioxidants can contribute to balance oxidative stress (Alkadi, 2020). Reactive oxygen species (ROS) includes molecule groups are derived from molecular oxygen.

Overproduction and the unbalanced mechanism of antioxidant protection system of ROS cause various diseases such as cancer, atherosclerosis, and coronary heart diseases etc. (Bursal et al.,2013). DNA damage induced by ROS has a slight specificity in the DNA helix. Damages caused by ROS at the DNA level; base modification, covalent bonding of bases in DNA or DNA-protein crosslinks, non-basic regions, and strand breaks (Lee and Dong, 2004).

ROS are weapons used by both the host immune system and antibiotics in antibiotic-mediated killing because it directly damages DNA, lipids, and proteins (Li et al., 2021).

Antibiotics are medicines which fight bacterial infections. Antibiotic resistance is a phenomenon which occurs when group of a bacteria are evolved, and they have ability to defeat the drugs designed to kill them (WHO, 2020). World Health Organization (WHO) report states that all of the world must change the way antibiotics uses. Antibiotic resistance when bacteria change so antibiotics no longer work in people who need them to treat infections is now a major threat to public health (Dorman et al., 200; Tabatabaei et al., 2015).

In this study, the protective effect of the fruit extract of the medlar plant obtained from Beyşehir district of Konya province against the damage caused by H2O2 and UV light was investigated. The results showed that antioxidant capacity of methanolic extracts obtained from medlar fruits and seeds by using

DPPH assay. Total phenolic content of medlar plant was analysed by using Folin-Ciocaltaeu method and we determined that antimicrobial activity of methanolic extract obtained from M. germanica fruits and seeds against 16 different bacteria by the microdilution method.

2. METHODS

2.1. Plant Material and Extract

Medlar were collected from a village of Beyşehir (Konya Province, Turkey). M. germanica extracts were prepared from fruits and seeds using the procedure described by (Badavi et al., 2008) found with some modifications. Fruits and seeds were manually separated. Seeds were desiccated by placing about 25-30°C temperature in the dark for a week and ground to a fine powder. This powder and fruits were stirred in methanol (70%) at room temperature for 3 days at room temperature with frequent agitation and filtrated after this. Then dried at room temperature (25-30°C) to evaporated methanol and then obtained a dry extract as a powder. After this process, the extracts to be used in the study were dissolved in sterile water at three different concentrations (60 mg/ml, 30 mg/ml and 10 mg/ml) to prepare a solution. The extracts of medlar were sterilized by filtration and stored in the refrigerator at +4°C.

2.2. Determination of Total Phenolic Content

The total phenolic content (TPC) was determined using the Folin Ciocalteu method with slight modification (Slinkard and Singleton, 1997). To carry out the analysis, firstly the Folin-Ciocalteu (FC) reagent was prepared by mixing 1 mL of FC Phenol solution with 30 mL of deionised water and this mixture vortex vigorously and incubate 3 min at room temperature. Then 0.25 mL sample solution was mixed with diluted Folin-Ciocalteu reagent (1 mL, 1:9), vortex vigorously and was allowed to stand for five min at room temperature. After incubation time 0.75 mL of 1% Na2CO3 was added and incubate for 2h at room temperature. The absorbance was measured at 760 nm at the end of the incubation period and the results were expressed as mg GAE/g using a gallic calibration curve.

2.3. Determination of Free Radical Scavenging Activity (DPPH)

The medlar extract was evaluated for 1, 1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity by following the method of (Sarikurkcu, 2011) with some adjustments. Approximately 1 mL of the diluted extract sample was added to a 4 ml of a 0.004% methanol solution of DPPH reagent and incubated for 30 m at room temperature at dark. The mixture absorbance was noted at 760 nm after 2h incubation at room temperature in dark. The DPPH radical scavenging activity results was expressed as mg of Trolox equivalents (TE) per gram of sample.

2.4. Determination of Antimicrobial Activity

The antimicrobial potentiality assay of the extracts was determined with minimal inhibitory concentration (MIC) test by using microdilution techniques (Zgoda and Porter, 2011). This assay was determined against the tested microorganisms. These were *Staphylococcus epidermidis* ATCC 12228, *Staphylococcus aureus* NCCT 8325, *Staphylococcus aureus* ATCC 25923, *Staphylococcus aureus* ATCC 6538, *Klebsiella pneumoniae* ATCC 70603, *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC 35218, *Escherichia coli* O157: H7, *Streptococcus salivarius* RSHE 606, *Streptococcus mutans* NTCC 10449, *Bacillus subtilis* ATCC 6633, *Bacillus cereus* ATCC 21778, *Pseudomonas aeruginosa* ATCC 27853, *Pseudomonas aeruginosa* ATCC 29853, *Salmonella typhimurium* ST10, *Enterococcus faecalis* ATCC 29212, that are obtained from the Selcuk University.

Bacterial cultures were performed by agar well diffusion method in Mueller Hinton Broth (MHB,Merck) plates for overnight at 37°C to adjust the turbidity to 0.5 McFarland standards giving a final inoculum of 108 CFU/ml. The two-fold serial of dilutions of extracts which highest concentration 64 mg/ml range from 32 mg/ml to 0.03 mg/ml were prepared in Dimethyl Sulfoxide (DMSO) of 25%. Serial solutions of the extracts were performed at microtitration petris. Each well was filled with 100 µl microbial suspension but the last well containing serial dilutions of antibacterial agents without microorganisms was used for DMSO which were used as negative control and also Chloramphenicol (Sigma) used as positive control.

2.5. DNA Protective Effect

Plasmid DNA (PBR-322) was used to determine whether it had an inhibitory effect on DNA damage. This DNA was first exposed to ultraviolet (UV) light (366 nm wavelength for 10 minutes) and 30% H2O2 (hydrogen peroxide) separately to damage the DNA. While UV causes dimer formation between thymine bases in DNA, H_2O_2 is a toxic compound that occurs as a result of chemical reactions in cells, and this toxin damages DNA. Then, it was observed by electrophoretic method whether the extract prevented the damage caused by treating the extract at different concentrations with DNA, UV and H2O2. The images were taken by running the samples at 90 volts for 1 hour in 1% agarose gel.

3. RESULTS AND DISCUSSION

Several types of natural antioxidants like phenolic compounds are found in nature and these are managed as scavengers of free radicals and could efficiently reduce the harmful effects of health of oxidative damage. Phenolic acids are present in a general of herbs and other species of the plant which are comprise a group of natural phenolic compounds (Kiokias et al., 2020). Phenolic acids have potential protective function against various diseases like stroke, coronary heart disease and cancers,

cardiovascular diseases, and inflammation (Gülçin et al., 2011). In this study, it was revealed that the total phenolic contents of methanolic extracts of M. germanica seeds (22.94 mg GAE/g extract) were higher than fruits (4.67 mg GAE/g extract). DPPH assays are widely used to analysis antioxidant activity because of it is an easy, rapid, and stable (Ercisli et al., 2012). So, DPPH assay was used determine free radical scavenging activity of medlar extracts. In this study, the seed of medlar extract (9.33 mg TE/g extract) exhibited stronger free radical scavenging activity in DPPH assay as compared to fruit extract (6.67 mg TE/g extract). These results indicate that M. germanica have moderate antioxidant capacity. Contrary to these results, several previously study reported that has been described a good antioxidant capacity for M. germanica (Gülçin et al., 2011; Ercisli et al., 2012; Campanella et al., 2003; Serteser et al., 2008).

In this study, while the extract of M. germanica obtained from seeds used in study did not have any effects against bacteria, it was shown that the fruit extract was effective against five bacteria (*B. subtilis* ATCC 6633, *B. cereus* ATCC 21778, *P. aeruginosa* ATCC 27853, *E. faecalis* ATCC 29212) in 32 mg/ml concentration and against eleven bacteria (*S. epidermidis* ATCC 12228, *S. aureus* NCCT 8325, *S. aureus* ATCC 25923*, S. aureus* ATCC 6538, *K. pneumoniae* ATCC 70603, *E. coli* ATCC 25922, *E. coli* ATCC 35218, *E. coli* O157:H7, *S.* salivarius RSHE 606, *S. mutans* NTCC 10449, *P. aeruginosa* ATCC 29853, *S. typhimurium* ST10) in 64 mg/ml concentration. This study is the first antimicrobial study with M. germanica fruit. However, there have been several recent studies with other parts of M. germanica (Tabatabaei-Yazdi et al., 2015; Campanella et al., 2003). Our results agree with these studies for antimicrobial activity of M. germanica. Obtained results showed that medlar extracts have informative data against bacterial microbial infections. Just the same clinical application of medlar plants needs more studies and successful and standardization of results. Medlar plants can use as an alternatively of inactive antimicrobial drugs currently used.

In this study, it has been determined by electrophoretic method that UV and H2O2 applied separately damage DNA, but when both are applied together, they cause more damage. It was observed electrophoretically that the medlar fruit extract protected DNA against these damages with the addition of DNA+UV, DNA+ H_2O_2 and DNA+UV+H_2O_2 to all three treatments (Fig. 1).

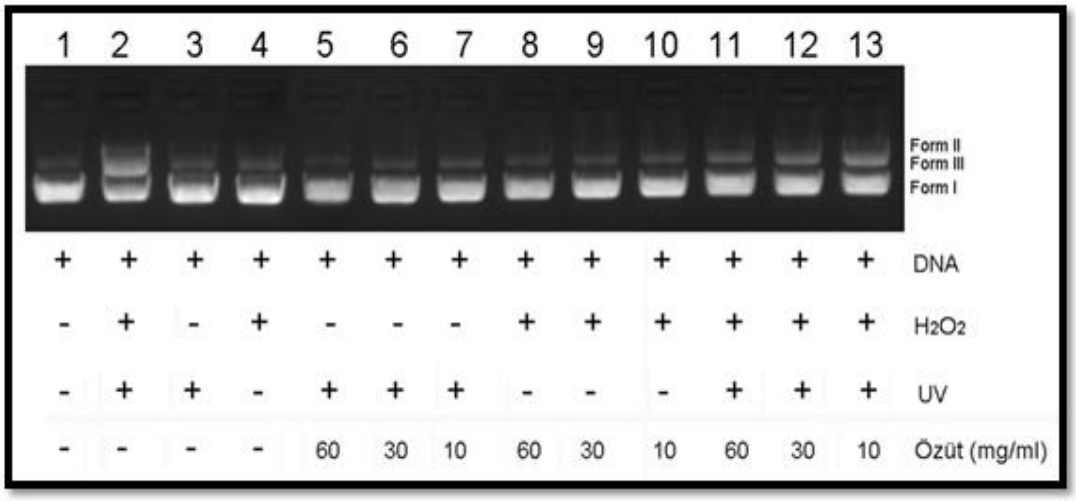

Figure 1. Agarose gel electrophoresis view. (The top, the bottom and in the middle bands indicate form II (open circular), form I (covalently closed circular) and form III (linear) plasmids, respectively.

Hydrogen peroxide (H_2O_2), produced by different metabolic processes during normal cell respiration and responsible for oxidative stress, is a well-known genotoxic agent that can induce oxidative DNA damage, including DNA breakage and base (Halliwell and Aruoma, 1991). Oxidative DNA damage induced by ROS plays a role in mutagenesis and carcinogenesis and leads to many human diseases, including cancer. For this reason, it has attracted great attention in recent years. In this study, it was determined that the fruit extract obtained from the medlar showed an important protective feature against DNA damage caused by H_2O_2 (Halliwell and Aruoma, 1991; Yang et al., 1999; Gill et al., 2011). In normal cell processes, cells can neutralize the harmful effects of reactive oxygen species and free radicals with several intracellular and extracellular antioxidant systems. Any change in any of these systems disrupts this balance leading to oxidative stress, resulting in an overall increase in cellular levels of ROS, which initiates lipid peroxidation and damages cellular macromolecules (lipids, proteins, and DNA), especially inducing oxidative DNA damage (Lee and Hae-Dong, 2004; Metgud and Saumya, 2014; Silihe et al., 2017). Antioxidants are compounds used in effective scavenging of free radicals and suppressing the effects of reactive oxygen substances. The lipid peroxidation products formed in various biochemical reactions are normally cleared by antioxidants (Lobo et al., 2010).

Ramos et al. (2010) investigated the protective effect of rosmarinic acid on cellular DNA in CaCo-2 and HeLa cells. Looking at the results of this study, it has been shown that rosmarinic acid (50 µM concentration), which has antioxidant properties, has a protective effect on CaCo-2 cells after 24 hours of incubation, and protects its genetic material against damage caused by H2O2 (Ramos et al., 2010). Vostálová et al. (2010) determined that rosmarinic acid (0.18-1.8 mg/l concentration) reduced UV-B-

induced DNA breakage in HaCaT keratinocytes by apoptotic process. It is possible to increase the number of reports on this subject (Psotova et al., 2006; Vatttem et al., 2006; Silva et al., 2008; Vostálová et al., 2010). The results of our study are also compatible with the results of these studies.

4. CONCLUSIONS

Most of the studies to determine the biological activity potentials of plant species are based on crude extracts and/or essential oils. Recently, active phytochemicals to elucidate their absolute potential are more interested in the food and pharmaceutical industries. Phenolic acids which are active phytochemicals are important because of their wide distribution in the plants. Phenolic acids are found in most fruits and vegetables that make up an important part of our diet. This study documented the antioxidant and DNA damage protection potentials of ten widely distributed phenolic acids. Our study shows that since the extract of the medlar fruit protects against DNA damage, protection from the harmful UV rays of the sun can be provided by adding it to sunscreen creams. Because it has been determined in scientific studies that the UV radiation of the sun damages the DNA in skin cells and causes skin cancer. Again, the extract of this fruit may also have a protective effect against damage due to oxidative stress.

Supporting Organization

"There is no person/organization that financially supports the study."

Conflict of Interest

"The authors have no conflict of interest."

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