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ARAŞTIRMA MAKALESİ **RESEARCH PAPER**

Antibiofilm, Antidiabetic and Antioxidant Potentials of *Vitis labrusca* L. Skin Extracts

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Abstract: This study examined the antioxidant, antimicrobial, antibiofilm, and α-glucosidase inhibitory activities and the total phenolic and flavonoid contents of the methanol, 50:50% methanol:water, and water extracts from *Vitis labrusca* L. skin parts. The 50:50% methanol:water extract exhibited the highest antioxidant activity, exhibiting 153 µM TEAC and 0.0947 mg/mL SC_{50}, as determined by the FRAP and DPPH• radical scavenging assays, respectively. Furthermore, the 50:50% methanol:water extract exhibited the highest total phenolic content and α-glucosidase enzyme inhibition among the other solvent extracts, with 141 µg/mL of GAE and an IC_{50} value of 0.103 mg/mL, respectively. The MIC values of the methanol, water and 50:50% methanol:water extracts were determined as 6.25, 25 and 12.5 mg/mL, aganist to clinical antibiotic resistance *Acinetobacter baumanii* respectively. The methanol, water and 50:50% methanol:water extracts were found to reduce the biofilm-forming capacity of the *Acinetobacter baumannii* isolate by approximately 1.7, 1.6 and 1.3-fold, respectively. The findings indicated that the 50:50% methanol:water extract exhibited the highest phenolic content, antioxidant activity, and α-glucosidase inhibition, whereas the methanol extract demonstrated the most pronounced antimicrobial and antibiofilm activities. The results of our research demonstrate that the utilization of diverse solvents and their respective compositions has the capacity to impart considerable variations in biological activity. This suggests the potential for *V. labrusca* skin components to serve as a valuable avenue in addressing ailments pertaining to oxidative stress and bacterial infections.

Keywords: Antibiofilm, antioxidant activity, α-glucosidase, *Vitis labrusca*.

Vitis labrusca L. Kabuk Ekstraktlarının Antibiyofilm, Antidiyabetik ve Antioksidan Potansiyelleri

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Öz: Bu çalışmada, *Vitis labrusca* L. bitkisinin kabuk kısımlarından elde edilen metanol, 50:50% metanol:su ve su ekstraktlarının antioksidan, antimikrobiyal, antibiyofilm ve α-glukozidaz inhibitör aktiviteleri ile toplam fenolik ve flavonoid içerikleri incelenmiştir. 50:50% metanol:su özütü, sırasıyla FRAP ve DPPH• radikal süpürücü analizleriyle belirlendiği üzere, 153 µM TEAC ve 0,0947 mg/mL SC_{50} ile en yüksek antioksidan aktiviteyi sergilemiştir. 50:50% metanol:su ekstraktı, sırasıyla 141 µg/mL GAE ve 0,103 mg/mL IC_{50} değeri ile diğer çözücü ekstraktları arasında en yüksek toplam fenolik içeriği ve α-glukozidaz enzim inhibisyonunu sergilemiştir. Metanol, su ve 50:50% metanol:su ekstraktlarının MİK değerleri, klinik antibiyotik direnci olan *Acinetobacter baumanii*' ye karşı sırasıyla 6.25, 25 ve 12.5 mg/mL olarak belirlenmiştir. Metanol, su ve %50:50 metanol:su ekstraktlarının *Acinetobacter baumannii* izolatının biyofilm oluşturma kapasitesini sırasıyla yaklaşık 1.7, 1.6 ve 1.3 kat azalttığı bulunmuştur. Bulgular, 50:50% metanol:su ekstraktının en yüksek fenolik içerik, antioksidan aktivite ve α-glukozidaz inhibisyonu sergilediğini, metanol ekstraktının ise en belirgin antimikrobiyal ve antibiyofilm aktivitelerini gösterdiğini ortaya koymuştur. Araştırmamızın sonuçları, çeşitli çözücülerin ve bunların ilgili bileşimlerinin kullanımının biyolojik aktivitede önemli farklılıklar yaratma kapasitesine sahip olduğunu göstermektedir. Bu durum, *V. labrusca* kabuk bileşenlerinin oksidatif stres ve bakteriyel enfeksiyonlarla ilgili rahatsızlıkların ele alınmasında değerli bir yol olarak hizmet etme potansiyeline işaret etmektedir.

Anahtar kelimeler: Antibiyofilm, antioksidan aktivite, α-glukosidaz, *Vitis labrusca*.

INTRODUCTION

The study of natural resources containing biologically active components has been a particularly prominent field of research in the recent years. This is particularly evident when considering the growing interest in health and healthy nutrition. Natural food products with a high nutritional value play an important role in the maintenance of human health. Fruits are natural foods that are rich in bioactive compounds such as vitamins, minerals and polyphenols. Thanks to their active ingredients, they can positively affect human health (Shashirekha et al., 2015). It is known that a number of different phytochemical components, including phenols, flavonoids, and carotenoids, are capable of scavenging and hinder of free radicals, including reactive oxygen species (ROS) (Husain & Kumar, 2012). It is widely acknowledged that many fruits are able to scavenge and hinder the formation of free radicals, which induce oxidative damage to biomolecules due to the antioxidant activity of their secondary metabolites. In addition, plant derived natural antioxidants are preferred over synthetic alternatives due to their favorable safety profiles (Nirmala et al., 2018).

Grape (*Vitis* L.), a member of the Vitaceae family, is one of the most widely consumed fruits worldwide, with a significant production volume. The most well-known and cultivated species within the *Vitis* genus are *Vitis labrusca* and *Vitis vinifera* (Trindade et al., 2016). Grapes can be consumed in their fresh or dried state, and they can also be used to produce wine, jam, grape juice, jelly, grape seed extract, vinegar, and grape seed oil (Granato et al., 2016). Grape exhibit high antioxidant and anticancer properties, which can be thanks to the phenolics, flavonoids, and anthocyanins found in their skin, flesh, and seed extracts (Cui et al., 2019). The grape has also been utilized in traditional medicine to treat a multitude of ailments due to its diverse biological activities (Liu et al., 2012). The variety of uses and the high phenolic content make the grapes very valuable.

Türkiye is an appropriate location for the cultivation of *V. vinifera* L. and *V. labrusca* L. varieties of grapevine. The genotypes of the *V. labrusca* species are widely cultivated in the Black Sea region. The plant's suitability for a rainy and humid climate, coupled with its durable structure, has permitted its cultivation in this region (Tahmaz et al., 2022). The hard and thick skin of the fruit, coupled with its large number of seeds, presents a significant obstacle to its consumption. The most common way to consume grapes is to squeeze them and remove the skin. The skin, which is easily removed, is not usually consumed.

Diabetes mellitus (DM) is one of the most prevalent metabolic disorders, characterized by deficiency or diminished effectiveness of insulin (Orhan et al., 2016). α-Glucosidase (EC 3.2.1.20) is an intestinal enzyme that catalyzes the break of the glycosidic bond in oligosaccharides into α-glucose (Safithri et al., 2016). Thus, an α-glucosidase inhibitor may be beneficial in the treatment of obesity and DM. It is therefore of great importance to identify novel natural α-glucosidase inhibitors against diabetes.

A significant public health concern worldwide is the high resistance of Gram-negative bacteria to antibiotics. The research and develop more effective natural antibacterials is crucial in order to combat the bacterial infections caused by pathogens.

It has been reported that grape seed proanthocyanidins, can act as anticarcinogenic agents (Nandakumar et al., 2008). Moreover, previous studies have demonstrated that grape seeds and skin extracts contain considerable levels of bioactive compounds (Rockenbach et al., 2011). Another study demonstrated that *V. vinifera* leaf extracts exhibited notable antimicrobial effects against several pathogenic bacteria (Moldovan et al., 2020). Another study has indicated that *Vitis vinifera* leaves may possess the ability to lower blood glucose levels in individuals with diabetes (Orhan et al., 2006).

Although there are numerous studies on the biological activities of *V. vinifera* varieties, the number of studies on *V. labrusca* genotypes remains limited. A review of the literature revealed that no study had been conducted to evaluate the antibiofilm and α-glucosidase inhibitor activities of the *V. labrusca* genotype. The goal of the present study was to evaluate the antibiofilm, antioxidant, antimicrobial and antidiabetic activities of various solvent (methanol, 50:50% methanol:water and water) extracts of *V. labrusca* skin parts.

MATERIAL AND METHOD

Plant material and sample preparation: The grape variety *V. labrusca*, which was harvested in Sürmene, Trabzon, Turkey in September 2023, was collected for analysis. The skins of the grapes were removed from the pulp. Then, over a period of four months, the skins were dried at ambient temperature. The dried samples were pulverized using a grinder. Following this process, the pulverized samples were extracted with solvents (methanol, 50:50% methanol:water and water) in a shaker for a period of two hours. Prior to analysis, the extracts were filtered through 0.45 µm syringe filters (Whatman), thus producing clear solutions. In order to evaporate the solvents at low pressure, a rotary evaporator

was utilized. All extracts were dissolved in their own solvents to the desired concentrations. The extracts were maintained at a temperature of 4°C until further utilization in subsequent experiments.

Determination of Antioxidant Activities

DPPH radical scavenging activity: The DPPH radical scavenging activities of extracts of skin parts of *V. labrusca* were investigated using the method described by Brand-Williams et al., (1995). The test concentrations of skin parts of *V. labrusca* extracts were adjusted to yield results with scavenging activity at concentrations providing approximately 50% of the maximal effect. The methodology involved mixing the extracts with a DPPH solution, maintaining the mixture at ambient temperature and in the absence of light for 50 minutes. The alterations in the absorbance of the DPPH radical following treatment with a standard antioxidant and extracts were quantified at a wavelength of 517 nanometers. A graph was generated based on the concentrations that corresponded to the absorbance values determined. The amount of sample required to halve the concentration of DPPH was determined in mg/mL and expressed as the SC_{50} (half of maximal scavenging concentration) value in this graph. The scavenging capacity of the extracts was compared to that of the reference antioxidant, Trolox.

Ferric reducing antioxidant power (FRAP): The FRAP effects of the extracts were in vitro evaluated using the method described by Benzie and Strain (1996). Firstly, all extracts were diluted to a concentration of 1 mg/mL. Subsequently, 50 µL of each extract and standard solution were combined with 1.5 µL of freshly prepared FRAP reagent in separate test tubes. Following a 20 minute incubation period, the absorbance values were spectrophotometrically measured at 595 nm. The results were calculated in µM TEAC (Trolox Equivalent Antioxidant Capacity) by means of a standard curve prepared from Trolox solutions.

Determination of Total Phenolic and Flavonoid Contents

Total phenolic content (TPC): The total phenolic content of the skin parts of *V. labrusca* extracted using different solvents were measured using Folin-Ciocalteu reagent method, as described by Slinkard and Singleton (1977). Firstly, each extracts and standard solution were mixed Folin reagent (0.2 N) in the test tubes. Then, the 7.5% solution of Na_2CO_3 was added to the solution and it was vortexed. Subsequently, the tubes were stored for a duration of 120 minutes in ambient conditions. Spectrophotometric analysis was conducted at a wavelength of 765 nm to determine the values of absorbance.

A series of standard solutions of varying concentrations of gallic acid were prepared. The total phenolic contents of the extracts were calculated as gallic acid equivalents (GAE µg/mL) utilizing the linear function of the standard calibration graph.

Total flavonoid content (TFC): The total flavonoid content of the skin parts of *V. labrusca* extracts was quantified in accordance with the method of Fukumoto and Mazza (2000).

A series of standard solutions of varying concentrations of quercetin were prepared. The total flavonoid substance amounts of the extracts were calculated as quercetin equivalents (QAE µg/mL) utilizing the linear function of the standard calibration graph.

Determination of Antimicrobial Activity

Determination of minimum inhibitory concentrations of extracts: The minimum inhibitory concentration (MIC) of the skin parts of *V. labrusca* extracted with different solvents were investigated by the liquid microdilution method against the clinically antibiotic-resistant *Acinetobacter baumannii* isolate. Experiments were performed in triplicate and on 96 well plates with an initial concentration of 50 mg/mL of the extracts (Çimen & Düzgün, 2020).

Investigation of antibiofilm properties of extracts: After determining the MIC value of the extracts, 1/2 MIC value was used in the biofilm experiment. The antibiofilm effect of skin parts of *V. labrusca* extracts were investigated on the clinical isolate *A. baumanii*, which has previously determined biofilm-forming capacity. Antibiofilm experiments were performed using the semi-quantitative crystal violet staining method. All experiments were performed in a 96 well plate and in triplicate. *Escherichia coli* Dh5@ (Ac) strain was used as a control in the experiments. Considering that the control strain did not form biofilm, the evaluation was made according to four different criteria: 1. A≤Ac Negative, 2. Ac<A≤2Ac Weak positive, 3. 2Ac<A≤4Ac Moderately positive, 4. A>4Ac Strong positive (Çimen & Düzgün, 2020).

Determination of Enzyme İnhibition

α-Glucosidase inhibition assay: The α-glucosidase enzyme activity of skin parts of *V. labrusca* extracts were investigated through a modification of the standard methodology (Yu, et al., 2012). Initially, 650 µL of phosphate buffer (pH: 6.8 and 0.1 M) was added to the tubes. Subsequently, 20 µL of the sample and 30 µL of the enzyme (*Saccharomyces cerevisiae*, lyophilised powder, ≥ 10 units/mg protein) were added. Following a 10-minute incubation period at 37 °C, 75 µL of substrate, 4-nitrophenyl α-D-glucopyranoside, was added to the mixture. After a 20 minute wait at the same temperature, 650 µL of 1 M Na_2CO_3 was added to the tubes, after which the absorbance values were measured on a UV/VIS spectrophotometer.

Acarbose was studied in different concentrations as the standard inhibitor. The study was conducted in three experimental groups. The IC_{50} values of acarbose and the samples were calculated (Kardil et al., 2024).

RESULTS AND DISCUSSION

Evaluation of antioxidant activity

In this study, DPPH and FRAP methods were used to determine the antioxidant activities of skin parts of *V. labrusca* extracts. The SC_{50} values, which represent the antioxidant activity of the extracts in terms of their capacity to scavenge DPPH radicals, are presented in Figure 1. All extracts exhibited concentration-dependent scavenging activities against the DPPH radical. The DPPH radical scavenging assay indicated that the 50:50% methanol:water extract of skin part of *V. labrusca* exhibited highest antioxidant activity, with an SC_{50} value of 0.0947 mg/mL, while the water extract demonstrated the lowest activity, with an SC_{50} value of 0.1953 mg/mL. In a previous study, Santos et al., (2011) reported that the SC_{50} values of DPPH radical scavenging activity in skin parts of grape methanolic extract was 234.53 µg/mL. The results of this study were comparable to those obtained in our own study. In another study, Rockenbach et al., (2011) reported that the SC_{50} values of DPPH radical scavenging activity in skin parts of grape methanol/water/acetic acid (80:20:5) extract was 3640 µmol of trolox equivalence per 100 grams of dry weight (µmol TE/100 g dw).

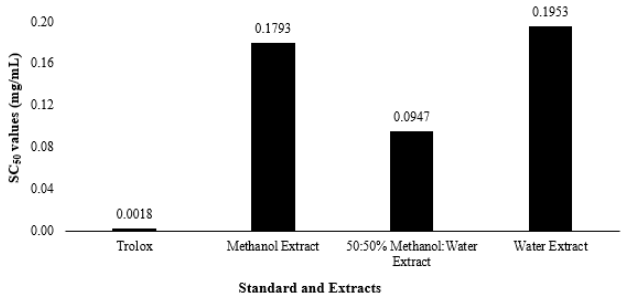

Figure 1. The SC_{50} values of skin parts of *V. labrusca* extracts.

The FRAP activities of the extracts are presented in Figure 2 and expressed as µM TEAC. The 50:50% methanol:water extract of skin parts of *V. labrusca* had the highest reducing activities, with 153 µM TEAC, while methanol and water extracts were 116 and 58 µM TEAC, respectively. In a study conducted by Rockenbach et al., (2011) it was demonstrated that the skin part of the Isabel grape exhibited reducing activities with a value of 4362 µmol Fe^{2+}/100 g dw. In another study, Dealindo et al., (2019) reported that 60% ethanolic extract of grape skin exhibited reducing activities with a value of 2627 mg ascorbic acid equivalence per 100 grams of dry weight (mg AAE/100 g).

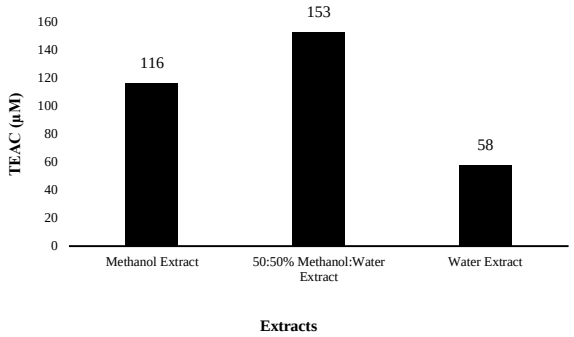

Figure 2. TEAC (µM) values of the skin parts of *V. labrusca* extracts.

Determination of total phenolic and flavonoid contents: The phenolic compounds, reactive oxygen species (ROS) scavengers, are responsible for many biological activities and including protection against such as cardiovascular diseases, atherosclerosis, hypertension, cancer, diabetes and neurological problems. The grape skins are the principal source of grape phenolic compounds, and the content of these compounds is subject to variation depending on the grape variety (Cosme et al., 2018). In the present study, the methanol:water extract of the skin parts of *V. labrusca*, prepared at a ratio of 50:50, exhibited the highest total phenolic content, with a value of 141 µg/mL GAE (Figure 3). In the literature, Rockenbach et al., (2011) reported that among the grape varieties subjected to analysis, the Isabel variety exhibited the highest concentration of phenolic compounds in the skin, with values reaching 1839 mg of catechin equivalence per 100 grams of dry weight (mg CE/100 g dw). According to the results of Santos et al., (2011) reported that the total phenolic contents of the skin parts of different grape species exhibited variation, with values ranging between 1.43 and 2.46 mg/g EAG. They also identified the Isabel variety as having the highest concentration of phenolic compounds in its extract.

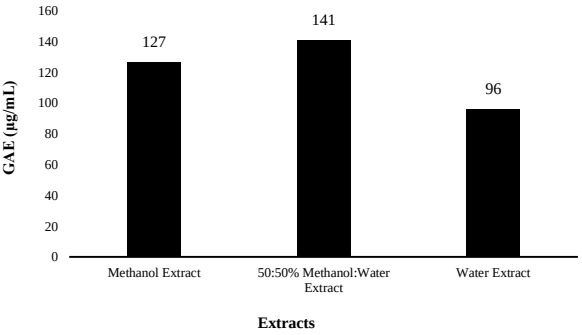

Figure 3. The TPC values of skin parts of *V. labrusca* L. extracts (µg/mL GAE).

Flavonoid compounds, which are secondary metabolites, are bioactive compounds that provide diverse benefits for human health (Raffa et al., 2017). In the present study, the flavonoid content of the methanol extract

derived from the skin parts of *V. labrusca* was found to be 0.057 µg/mL QAE. In solvent extracts containing either 100% or 50% water, precipitation was observed at the concentrations at which flavonoids were detected. In the literature, Deolindo et al., (2019) reported that the flavonoid content of 60% ethanolic extracts of grape skin was found to be 1504 mg of catechin equivalence per 100 grams of dry skin weight (mg CE/100 g fw). Kurt-Celebi et al., (2020) reported that the flavonoid content in the grape was affected by berry development. The study additionally revealed that the flavonoid content of overripe grape skin reached 93 mg of quercetin equivalence per 100 grams of fresh weight (mg QE/100 g fw).

The solvent composition resulted in notable alterations to the antioxidant activities of *V. labrusca* skin extracts. The methanol:water extract, prepared at a ratio of 50:50, demonstrated the most pronounced antioxidant activity and phenolic content. Akar et al., (2020) reported that the antioxidant activity of the extracts, which are typically composed of 50% methanol and 50% water, was found to be superior to that of the 100% methanol and 100% water extracts. The results of this study were found to be consistent with those of our own study. The findings revealed a positive correlation between the antioxidant activity of DPPH and FRAP, as well as the total phenolic content (TPC), of the skin parts of *V. labrusca* extracts.

Evaluation of antimicrobial activity: Against the clinical antibiotic resistant *A. baumanii* isolate, the MIC value of the 50:50% methanol:water extract of skin part of *V. labrusca* was determined as 12.5 mg/mL, of the extract with water was 25 mg/mL and of the methanol extract of *V. labrusca* was determined as 6.25 mg/mL (Table 1). The results indicated that the extraction of *V. labrusca* with methanol had the lowest MIC value and the highest antimicrobial activity. In the literature many studies have been conducted that methanol extracts prepared from various plants have higher antimicrobial activity compared to other solvents (Mothana et al., 2005; Debnath, 2008; Vadlapudi, 2010; Mabadahanye, 2022). The fact that crude extracts obtained with methanol gave quantitatively better results than other solvents is an indication of the high bioactivity of methanol extracts (Njume et al., 2011). Following the determination of MIC values for the extracts, the 1/2 MIC value was utilized in antibiofilm experiments. Antibiofilm experiment was performed by semi-quantitative crystal violet staining method. The antibiofilm activity of the extracts was evaluated based on the OD value (Ac: 0.1915) of the biofilm-forming capacity of the control isolate (*E. coli* Dh5@). Considering the biofilm-forming capacity of the control strain, it was observed that the *A. baumannii* clinical isolate had a moderate biofilm-forming capacity. When the antibiofilm activity results of the extracts were examined, it was determined that the extracts extracted with all three different solvents weakened the biofilm-forming capacity of the strain, which had a moderate biofilm-forming capacity (Table 1).

Table 1. MIC and antibiofilm results of the *V. labrusca* L. skin extracts.

	MIC Value (mg/mL)	Biofilm Value / OD
50:50% Methanol:Water	12.50	0.3216
Water	25.00	0.2632
Methanol	6.25	0.2417
A. bumannii	-	0.4132
E. coli Dh5@ (control)	-	0.1915

Antibiotic resistance is a major public health problem worldwide, with significant numbers of people affected each year. Biofilm formation in bacteria also contributes to the formation of antibiotic resistance. Special importance is given to studies on *A. baumannii* isolates with biofilm-forming capacity and high multidrug development potential (Mumtaz et al., 2023; Nasution et al., 2023). Fighting antibiotic resistance becomes more difficult because the development of new antibiotics takes a long time and is costly. Identification of new antimicrobial agents is required to treat infections. Consequently, plant extracts, which are a valuable source of bioactive compounds, play an important role as a novel strategy in the fight against pathogenic microorganisms (Manso et al., 2021). In a recent study, Silva et al., (2023) posited that plant-based products or their derivatives may serve as a promising therapeutic strategy for the eradication of bacterial biofilms and the associated infections. Moreover, it was stated that flavonoids and phenolic compounds appear to be the most efficacious against bacterial biofilms. In another study, Shamim et al., (2023) reported that phenolics and flavonoids are among the natural components that exhibit potent anti-biofilm properties. Therefore, in this study, the antimicrobial and antibiofilm activity of grape extracts against the multidrug-resistant clinical *A. baumannii* isolate was investigated. As a result, it is thought that extract of skin part of *V. labrusca* extracts extracted with different solvents have antimicrobial and antibiofilm activities and therefore may be supportive for the treatment of multidrug-resistant *A. baumannii* infections. Further research is required to fully elucidate the mechanism of action of the plant extract, with a view to optimising the clinical application of these compounds in the treatment of biofilm-associated infections (Tapia-Rodriguez et al., 2023).

Evaluation of α-glucosidase inhibitory effects: The α-glucosidase enzyme activity of skin parts of *V. labrusca* extracts in different solvents (methanol, 50:50% methanol:water and water) was found to be 0.211 mg/mL IC_{50}, 0.103 mg/mL IC_{50} and 0.435 mg/mL IC_{50}, respectively (Table 2). The 50:50% methanol:water extract (0.103 mg/mL IC_{50}) demonstrated the highest enzyme

activity, while the water extract (0.435 mg/mL IC_{50}) exhibited the lowest activity.

A search of the literature revealed no studies on α-glucosidase enzyme activity conducted only on the skin of this species. A number of studies have been conducted on the α-glucosidase enzyme, which is commonly found in grape pomace, a byproduct of wine production (Cisneros-Yupanqui et al., 2023). In a study, the % enzyme activity of a different species, *V. vinifera* pomace, was extracted at different temperatures (90, 120, and 150°C) and with different solvents (water, glycerol and ethanol) and examined. The analysis of the extracts revealed that the water-ethanol extract obtained at 90°C exhibited significant inhibition of α-glucosidase (98%) at a concentration of 1000 µg/mL (Huamán-Castilla et al., 2021). In a separate study, the anti-diabetic properties of Merlot grape pomace extract (40:60% ethanol:water) were investigated. It has been demonstrated that this species, which is employed particularly in the beverage industry, exhibits enzymatic efficacy (Kato-Schwartz et al., 2020). Similarly, in our study, the water-methanol mixture showed a higher effect. This can be interpreted as the use of solvents in a process of extraction, whereby different secondary metabolites are introduced into the solvent in specific proportions.

Table. 2 α-Glucosidase Enzyme inhibition activity of *Vitis labrusca* L. skin extracts.

Sample	IC_{50} (mg/mL)	R^2
Acarbose	0.029 ± 0.02	0.9911
Water	0.435 ± 0.09	0.9899
50:50% Methanol:Water	0.103 ± 0.03	0.9909
Methanol	0.211 ± 0.04	0.9927

CONCLUSION

This study presented the antioxidant, antimicrobial, antibiofilm, and α-glucosidase inhibitory activities and the total phenolic and flavonoid contents of skin parts of *V. labrusca* extracts. The study demonstrated that the use of diverse solvent compositions resulted in the extraction of varying secondary metabolites and their dissolution into solution, leading to notable distinctions in biological activity. The methanol:water extract of the skin parts of *V. labrusca*, at a ratio of 50:50, demonstrated the highest antioxidant and α-glucosidase inhibitory activity, along with the greatest total phenolic content. Furthermore, a correlation was identified between antioxidant activity, total phenolic content, and α-glucosidase inhibitory effects. In contrast, the findings demonstrate that the methanol extract of the skin parts of *V. labrusca* exhibited the most pronounced antimicrobial and antibiofilm activity than the other extracts. This study demonstrated, for the first time, that the skin part of *V. labrusca* exhibited both an antibiofilm effect and α-glucosidase inhibitory activity. The findings of our investigation suggest that skin parts of *V. labrusca* may serve as a promising candidate for the prevention and treatment of diseases associated with oxidative damage and bacterial infections. Consequently, further research is required to corroborate these biological activities and elucidate the underlying mechanisms of action.

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Conflicts of Interest: The authors declare no conflict of interest.

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