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Antidiabetic and antioxidant properties of nine medicinal and aromatic plants extracts: Inhibition of key enzymes linked to type-2 diabetes

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Abstract

The study aimed to determine enzyme inhibitory activities and bioactive features of the methanol extracts of peppermint (*Mentha piperita* L.), spearmint (*Mentha spicata* L.), yarrow (*Achillea millefolium* L.), sage (*Salvia officinalis* L.), yellow cantoron (*Hypericum perforatum* L.), thyme (*Thymus vulgaris* L.), lavender (*Lavandula angustifolia* Mill.), lemon balm (*Melissa officinalis* L.) and echinacea (*Echinacea purpurea* L.). The methanol extraction was carried at 40 °C for 2 h. The inhibitory activities of plant extracts on antioxidant and α-glucosidase, α-amylase and lipase enzymes were determined. The antioxidant activities of these extracts were determined by the methods of DPPH, ABTS and β-carotene-bleaching test (βC). The results showed that peppermint significantly (p<0.05) inhibited the activity of α-glucosidase (IC_{50}: 1.18 ± 1.079 mg/mL) and DPPH free radical scavenging activity (EC_{50}: 2.36 ± 0.3). Total phenolic content (TPC) and total flavonoid content (TFC) of the extracts were between 3.06-31.13 mg gallic acid equivalents (GAE) and 0.58-4.39 µg catechin equivalents (CE) per g of plant, respectively. It concluded that all the plant materials used in the study had inhibitory effect on α-glucosidase.

Keywords: Antioxidant activity, medicinal plants, enzyme inhibitory activity, α-glucosidase

1. Introduction

Diabetes mellitus is a chronical disturbance defined by hyperglycaemia. Diabetes can cause a range of complications, involving many diseases [1]. Postprandial hyperglycemia is nearly associated with type 2 diabetes. Reducing the digestion and absorption of carbohydrates to control postprandial blood sugar is an effective strategy for preventing diabetes [2]. Miglitol, acarbose and voglibose are the most common drugs used in the treatment of hyperglycemia. These medicament s are involved in reducing the hydrolysis of carbohydrates and preventing postprandial hyperglycemia in diabetes mellitus [3]. But, these medicaments may display some negative impacts [4]. Inhibition of α-amylase, α-glucosidase and lipase enzymes has an important strategy in treating diabetes and obesity. Many studies have shown that α-glucosidase and α-amylase are effective in the treatment of diabetes by managing the assimilation and sorption of glucose [5]. Since the side effects that occur when synthetic drugs are used in the prevention of type 2 diabetes are not found in native compounds obtained from foods, they may be preferred more [6].

It is well known that some chronic diseases and illnesses are caused by metabolic oxidative damage due to an excessive accumulation of free radicals [7]. On the other hand, antioxidants have most likely preventive effects against such detriment. Most of the medicinal and aromatic plants and their extracts are important antioxidant sources and can be used in treating and preventing many diseases [8]. In recent years, the use of traditional natural herbs and plants has been popular, and now are commonly available for consumption [9]. This has led to progressive research on analyzing herbs conventionally used by regional folk, studying their

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biological activities, and developing new-native alternate medicine formulations [10].

The aim of this study is to determine α-amylase, α-glucosidase and lipase inhibition activity, and antioxidant, total phenolic and total flavonoid contents of the methanol extracts obtained from nine medicinal and aromatic plants [peppermint (*Mentha piperita* L.), spearmint (*Mentha spicata* L.), yarrow (*Achillea millefolium* L.), sage (*Salvia officinalis* L.), yellow cantoron (*Hypericum perforatum* L.), thyme (*Thymus vulgaris* L.), lavender (*Lavandula angustifolia* Mill.), lemon balm (*Melissa officinalis* L.) and echinacea (*Echinacea purpurea* L.)].

2. Materials and Method

2.1. Materials

Peppermint (*Mentha piperita* L.), spearmint (*Mentha spicata* L.), yarrow (*Achillea millefolium* L.), sage (*Salvia officinalis* L.), yellow cantoron (*Hypericum perforatum* L.), thyme (*Thymus vulgaris* L.), lavender (*Lavandula angustifolia* Mill.), lemon balm (*Melissa officinalis* L.) and echinacea (*Echinacea purpurea* L.) were harvested from a farm field of Agricultural Research and Application Centre at Erciyes University (Kayseri, Turkey) in July. The material was open air dried at room temperature (~25 °C) for about 15 days without direct exposure to sunlight. Water was purified using a Millipore Simplicity 185 system (Merck, Darmstadt, Germany). The α-glucosidase, α-amylase and lipase were obtained from Sigma Aldrich Co. (St. Louis, MO, USA). The chemical substances, standards and other materials used in the work were of analytical grade and purchased from Sigma Aldrich Co. (St. Louis, MO, USA).

2.2. Methods

2.2.1. Extraction

The dried plant materials were chopped into small pieces and pulverized into a fine powder by using grinder. The plant materials (20%, w/v) were extracted with methanol in a shaking water bath (Nuve ST30, Turkey) at 40 °C for 1 h. The resulting mixture was passed through a coarse filter paper. The remaining portion of the filter paper again was extracted with methanol (100 mL) in a shaking water bath at 40 °C for 1 h. Each sample was transferred to the extracts previously collected in a balloon flask. All extracts were completed to 200 mL with methanol and stored at -18 °C until analysis.

2.2.2. Total phenolic content

Total phenolics contents (TPC) of the extracts were determined using the method of Singleton et al. (1998) [11]. A 2 mL of 10-fold diluted Folin-Ciocalteu's phenol reagent was mixed with 0.4 mL diluted extract or gallic acid solution (20–100 mg/L). A 1.6 mL sodium carbonate solution (7.5%, w/v) was added into the above mixture. After incubation at room temperature for 1 h, the absorbance was read at 765 nm using a spectrophotometer (Model UV-1700, Shimadzu Corp., Kyoto, Japan) and the results were expressed as mg gallic acid equivalent (GAE) per g of sample.

2.2.3. Total flavonoid content

Total flavonoid content (TFC) was determined using a colorimetric method [12]. In brief, aqueous methanolic extracts or catechin solutions (1 mL), distilled water (4 mL), 5% $NaNO_2$ (0.3 mL) and 10% $AlCl_3$ (0.3 mL) were mixed consecutively. After incubating the mixture for 6 min, 1 M NaOH (2 mL) was added and the volume was made up to 10 mL with purified water. The absorbances were measured at 510 nm by a spectrophotometer. Six different concentrations of catechin solutions (15–200 mg/L) were used for calibrations. The results were expressed as µg catechin equivalents (CE) per g of sample.

2.2.4. Radical scavenging activity by DPPH

DPPH assay was determined according to method of Singh et al. (2002) [13]. Briefly, a 0.1 mL of diluted extract solution was mixed with 3.9 mL of a 25 mg/L methanolic solution of DPPH and this mixture was vortexed for 10 s. After 30 min of incubation at room temperature, absorbance was measured at 515 nm using UV-Vis spectrophotometer (Agilent 8453, USA) versus prepared blank (methanol). The results were expressed as EC_{50} value which is defined as amount of sample necessary to decrease initial DPPH concentration by 50%. EC_{50} was expressed as gram of plant to gram of DPPH.

2.2.5. Antioxidant capacity by ABTS

The antioxidant capacity was determined by another radical called ABTS [14]. The solutions of ABTS (2.45 mM) and $K_2S_2O_8$ (12.25 mM) were mixed and incubated in darkness for 16 h to obtain stock solution of ABTS radical. The absorbance of the

ABTS solution was adjusted to 0.700 ± 0.005 at 734 nm just before the application of the assay. Extracts (20 µL) and ABTS solution (2 ml) were mixed and incubated in a darkness for 6 min. Trolox standards (40-200 mg/L) were prepared and reacted with ABTS as stated above in order to generate a linear regression equation. The absorbances were measured by a spectrophotometer at 734 nm. The results were given as mg Trolox equivalent per 100 g sample.

2.2.6. Anti-oxidant activity by β-carotene-linoleate

β-Carotene bleaching assay (βC) was determined according to method of Singh et al. (2002) [13]. 0.2 mg of β-carotene, 20 mg of linoleic acid and 200 mg of Tween-40 were dissolved in 0.2 mL chloroform. After removing chloroform under nitrogen flush for 5 min, 10 mL demineralized water was added with vigorous stirring to form an emulsion. Four milliliter of this solution was added to each tube containing 0.2 mL of diluted samples. The control samples were prepared by adding 0.2 mL of distilled water instead of samples. Absorbance was measured at 470 nm using UV-Vis spectrophotometer (Agilent 8453, USA) versus prepared blank which was prepared as β-carotene emulsion but without adding β-carotene. Mixtures were incubated at 50 °C in a water bath until the control sample was bleached (120 min). Tubes were cooled to room temperature and absorbance was re-measured. Final results were expressed as percent inhibition in β-carotene assay. β-Carotene-bleaching assay (βC) was using the following equation (1):

$$AA\% = 100\left[1 - \left(\frac{A_0 - A_t}{A_0^0 - A_t^0}\right)\right] \quad (1)$$

where A_0 is the absorbance of test sample at the zero time; A_0^0 is absorbance of control sample at the zero time; A_t is absorbance of test sample at 120 min; and A_t^0 is the absorbance of control sample at 120 min.

2.2.7. Assays of α-amylase, α-glucosidase and lipase

The activities of α-amylase and α-glucosidase [15], and lipase [16] were determined by a combination of enzymatic and colorimetric methods.

For α-glucosidase assay, 1250 µL 67 mM KH_2PO_4 (pH = 6.8), 50 µL diluted extract and 50 µL α-glycosidase solution (0.2 U/mL) were incubated at 37 °C in a water bath for 5 min. The reaction was started with the addition of 125 µL 10 mM 4-nitropheyl α-D-glucopyranoside solution. The reaction was stopped at 20 min with the addition of 2000 µL 0.1 M Na_2CO_3. The absorbance was measured at 400 nm.

For the α-amylase assay, 0.5 mL 1% (w/v) potato starch solution (Sigma Aldrich), 0.5 mL diluted extract and 0.5 mL 20 mM NaH_2PO_4 (pH = 6.9) were mixed and incubated at 37 °C for 5 min. The reaction was started with the addition of 0.5 mL α-amylase solution (0.5 U/mL). The reaction was stopped at 30 min with the addition of 0.5 mL color reagent containing equal volume of 5.31 M sodium potassium tartrate solution in 2 M NaOH and 96 mM 3,5-dinitrosalicylic acid solution. The mixture was sealed and kept on a boiling water bath for 10 min. The absorbance of the resulting orange-red colored solution was measured at 540 nm.

For the lipase assay, 800 µL 100 mM Tris buffer (pH = 8.2), 100 µL diluted extract and 300 µL lipase solution (10 mg/mL) were mixed and incubated at 37 °C for 2 hour. The reaction was started with the addition of 800 µL 4-nitrophenyl laureate solution (300 µg/mL). The absorbance of the resulting yellow colored solution was measured at 400 nm.

The above mentioned 3 assays were carried out in the presence of the extracts to determine their inhibition activities with the related key enzymes. The control (acarbose, orlistat) and blank (pure water) samples for each enzymatic assay were prepared in the same way by excluding the extract and the enzyme, respectively.

$$Enzyme\ inhibition\ (\%) = \left(\frac{Abs_{control} - Abs_{extract}}{Abs_{control}}\right) \times 100 \quad (2)$$

where $Abs_{control}$ = absorbance of the control, and $Abs_{extract}$ = absorbance of the solution containing extract.

Standard curves were prepared using concentrations of phenolics in the extracts against enzyme inhibition (%) values (2). Final results were calculated from the curves and expressed as IC_{50} values, the phenolic concentration of extract providing 50% inhibition of the enzymes' activities.

2.3. Statistical analysis

All experiments and analyses were performed in two repetitions and two parallel and the results were expressed as mean ± standard deviations. Analysis of variances (ANOVA) and a post hoc tests (Tukey)

were applied to the data at a significance level of $p<0.05$ using SPSS 22.0 (Version 22.0, SPSS Inc., Chicago, IL, USA) program.

3. Results and Discussion

3.1. Total phenolic content and total flavonoid content

TPC of all plant extracts are expressed in Table 1. The TPC of the extracts ranged from 3.06 to 31.13 mg GAE/g. There was a significant difference ($p<0.05$) between the TPC of some extracts. Among extracts, the highest TPC was found in peppermint. On the other hand, echinacea showed the lowest TPC which was ~10 fold lower than peppermint. TFC of the extracts ranged from 0.58 to 4.09 µg CE/g. The changes in flavonoid content of all extracts were statistically significant ($p<0.05$). Peppermint had the highest flavonoid content while the lowest was in *Echinacea* (Table 1). Yellow cantoron and sage also had high levels of TFC compared to other plant extracts. As shown in Table 1, linear relations were evaluated between TFC and TPC of leaves. The TFC and TPC of peppermint, yellow cantoron and sage were 4.09, 1.82, 2.33 µg CE/g and 31.13, 24.59, 21.75 mg GAE/g respectively. These differences were statistically significant ($p<0.05$). This is an expected case due to the fact that flavonoids are one of the major phenolic compounds.

TPC content of peppermint (31.13 mg GAE/g) determined in our study was competitively similar to and within the range of 29.42 [17] and 40.7 mg GAE/g [18]. Yi and Wetzstein (2010) reported on the TPC levels of the *Lamiaceae* plant family including thyme (20.7 mg GAE g^{-1}), rosemary (10.2 mg GAE g^{-1}), sage (15.1 mg GAE g^{-1}), spearmint (19.0 mg GAE g^{-1}), and peppermint (22.4 mg GAE g^{-1}) which were showed similar to our results [19]. Karadağ (2019) found similar TPC levels of sage (21.13 mg GAE/g), lemon balm (16.89 mg GAE/g) and spearmint (16.37 mg GAE / g) [20]. All these results were relatively similar to the results in this study.

3.2. Antioxidant activity

The results of antioxidant activity of plant extracts were expressed using the term EC_{50} (Table 2). The lower $EC5_0$ the higher antioxidant activity. Statistically significant differences ($p<0.05$) were observed between some extracts in their antioxidant activity. Of the nine plant extracts studied, peppermint (2.36 g of plant/g of DPPH), yellow cantoron (2.9 g of leaf/g of DPPH) and sage (4.06 g of plant /g of DPPH) exhibited the highest values of antioxidant activity while the lowest was observed in echinacea, yarrow, lavender (29.91, 23.05 and 19.1 g of plant /g of DPPH respectively). As seen in Table 2, β- carotene bleaching method (βC), ranking of the extracts with respect to their antioxidant activity was the same to the level obtained from DPPH assay. The βC of plants ranged from 31.80 to 59.08%. The sage showed the best in this assay with 59.08%, and this was followed by thyme and spearmint. Statistically significant differences ($p<0.05$) were found between the extracts in ABTS assay and DPPH activities (Table 2). However, thyme showed higher antioxidant capacity than peppermint in ABTS test. The different reaction mechanisms of the assays may affect the antioxidant results.

Table 1. Total phenolic contents and total flavonoid content of plant extracts

Plant extracts	TPC (mg GAE/g)	TFC (µg CE/g)
Sage	$21.75^{bcd} \pm 0.05$	$2.33^{e} \pm 0.13$
Yarrow	$5.66^{a} \pm 1.12$	$0.75^{ab} \pm 0.01$
Echinacea	$3.06^{a} \pm 0.98$	$0.58^{a} \pm 0.01$
Thyme	$15.65^{bc} \pm 4.11$	$1.04^{bc} \pm 0.01$
Lavender	$4.82^{a} \pm 0.65$	$0.81^{ab} \pm 0.01$
Lemon balm	$13.4^{abc} \pm 2.71$	$1.28^{c} \pm 0.001$
Spearmint	$12.85^{ab} \pm 1.49$	$1.69^{d} \pm 0.11$
Peppermint	$31.13^{d} \pm 1.85$	$4.09^{f} \pm 0.04$
Yellow cantoron	$24.59^{cd} \pm 4.22$	$1.82^{d} \pm 0.08$

GAE: gallic acid equivalent, CE: catechin equivalent; TPC: total phenolic content, TFC: total flavonoid content. Values that are followed by different letters within each line are significantly different ($p < 0.05$).

Table 2. Antioxidant activity of plant extracts

Plant extracts	DPPH EC_{50} (g /g DPPH)	ABTS (mg TEAC/g)	βC (AA%) (mg GAE/L)
Sage	$4.06^{ab} \pm 0.20$	$44.47^{cd} \pm 0.74$	$59.08^{c} \pm 6.11$
Yarrow	$23.05^{c} \pm 5.73$	$19.69^{ab} \pm 2.89$	$35.06^{ab} \pm 1.80$
Echinacea	$29.91^{c} \pm 10.11$	$5.74^{a} \pm 0.7$	$41.59^{bc} \pm 4.64$
Thyme	$14.57^{abc} \pm 3.82$	$73.33^{de} \pm 2.22$	$47.27^{a} \pm 2.16$
Lavender	$19.1^{bc} \pm 2.55$	$12.91^{ab} \pm 1.50$	$16.81^{bc} \pm 0.94$
Lemon balm	$5.4^{ab} \pm 0.6$	$31.44^{bc} \pm 2.14$	$41.46^{bc} \pm 0.83$
Spearmint	$5.77^{ab} \pm 0.26$	$34.13^{bc} \pm 3.9$	$47.48^{bc} \pm 4.18$
Peppermint	$2.36^{a} \pm 0.3$	$64.42^{e} \pm 2.26$	$39.73^{bc} \pm 2.72$
Yellow cantoron	$2.9^{a} \pm 0.7$	$53.63^{e} \pm 2.2$	$31.80^{ab} \pm 6.93$

Values that are followed by different letters within each line are significantly different ($p < 0.05$). TEAC: Trolox equivalent antioxidant capacity; GAE: gallic acid equivalent.

Albayrak et al. (2013) determined antioxidant activity of the Lamiaceae family species such as peppermint, thyme, lemon balm, basil, rosemary and sage. Methanolic extracts of thyme, lemon balm, basil, sage and peppermint were found EC_{50} = 21.91, 20.16, 41.80, 15.05 and 17.91 µg/mL, respectively [21]. Our results showed that the studied plants displayed important antioxidant properties. These effects are associated with the grades of total bioactive components from the plant extracts since it was also previously shown that there is a potent relation among total bioactive components and antioxidant features [22].

3.3. α-Glucosidase inhibition activity

None of the extracts showed inhibition against α-amylase and lipase enzymes. All extracts showed inhibition activity against α-glucosidase. Although there was a difference between peppermint, spearmint, yellow cantoron and sage in TPC, these extracts showed statistically no significant differences ($p>0.05$) in inhibition activity against α-glucosidase (Table 3). The antidiabetic activity of extracts determined as IC_{50} ranged from 1.18 to 47.45 mg/mL. The lower IC_{50} the higher antidiabetic activity. Peppermint (1.18 mg/mL) exhibited the highest values of α-glucosidase inhibition activity and this was followed by spearmint, yellow cantoron and sage (Table 3). These results show that plants and their parts are important to overcome metabolic diseases including diabetes. Nine plant extracts have shown a great potential of α-glucosidase inhibitor.

Çam et al. (2020) reported that the peppermint and spearmint extracts obtained using pressurized water extraction have α-glucosidase inhibition activity determined as 0.6 and 1.2 mg phenolic/mL [23]. Pavlić et al. (2021) showed that the peppermint essential oil obtained by different techniques has an inhibitory effect on α-amylase and α-glucosidase enzymes [24]. When comparing these results with our results, it can be speculated that the extraction method and the level of essential oil may affect the degree of inhibition activity. In our study, no inhibitory effect of sage against α-amylase and lipase was found, while Ercan and El (2018) showed that sage had the inhibitory activity against α glucosidase, α-amylase and lipase. This different may be due to the pure use of carnosic acid content in the study of Ercan and El (2018) [25].

Gonçalves (2017) reported that the methanolic extracts of the four aromatic plants showed significant inhibitory activity against α-glucosidase, but there was a weak activity against α-amylase [26]. The choosing inhibition of α-glucosidase is a chosen influence for plant extracts to control glucose grasp [27]. In fact, the plant extracts of numerous plants, including conventionally used plants were noticed to apply potent inhibition for α-glucosidase and insignificant effect for α-amylase activity [28]. Similarly all extracts did not affect α-amylase activity while inhibiting α-glucosidase enzyme.

Flavonoids have inhibitory potential against to lipase. The result indicated that plants rich in flavonoids would have a great potential of inhibiting lipase effectively [29]. It can be speculated that the extracts a not rich in TFC do not show lipase inhibitory effect, in our study.

Table 3. α-Glucosidase inhibitor activities of plant extracts

Plants extracts	IC_{50} (mg/mL)	IC_{50} (mg phenolic/mL)
Sage	$6.41^{a} \pm 0.28$	$0.14^{a} \pm 0.07$
Yarrow	$30.78^{b} \pm 3.75$	$0.81^{a} \pm 0.01$
Echinacea	$47.45^{c} \pm 0.03$	$0.15^{a} \pm 0.01$
Thyme	$12.41^{ab.} \pm 3.17$	$0.23^{a} \pm 0.06$
Lavender	$25.39^{b} \pm 7.1$	$0.12^{a} \pm 0.04$
Lemon balm	$14.77^{ab} \pm 4.9$	$0.2^{a} \pm 0.07$
Peppermint	$1.18^{a} \pm 1.079$	$0.04^{a} \pm 0.03$
Spearmint	$1.45^{a} \pm 0.28$	$0.07^{a} \pm 0.02$
Yellow cantoron	$3.32^{a} \pm 0.02$	$0.08^{a} \pm 0.02$

Values that are followed by different letters within each line are significantly different ($p < 0.05$). IC_{50}: The amount of substance that inhibits enzyme activity by 50%.

Table 4. Correlation coefficient among the levels of analyzed parameters

	TPC	TFC	EC_{50}	IC_{50}	ABTS	βC
TPC	1	0.83^{**}	-0.77^{**}	-0.88^{**}	0.94^{**}	0.36
TFC		1	-0.71^{**}	-0.72^{**}	0.69^{**}	0.26
EC_{50}			1	0.85^{**}	-0.63^{**}	-0.30
IC_{50}				1	-0.84^{**}	-0.23
ABTS					1	0.26
βC						1

** = correlation is significant at the $p < 0.01$. TPC= total phenolic content; TFC= total flavonoid content; βC= β- carotene bleaching assay; ABTS=Antioxidant capacity; EC_{50}= antioxidant activity; IC_{50}= α-glucosidase inhibition

3.4. Correlation

Pearson's correlation coefficients between the means of each variable were established in our study. Statistically significant (p<0.01) correlation coefficient were observed among several bioactive compounds obtained in this study (Table 4).

As expected, the highest correlation coefficient were found between TPC and ABTS values (R^2=0.94). Phenolic compounds seem to be the main class of phytochemicals in nine medicinal plants. These secondary metabolites could be responsible for an antioxidant potential. The correlation coefficient between phenolic compounds and antioxidant (EC_{50}) and α- glucosidase inhibition (IC_{50}) activity was found to be R^2 = -0.77 and -0.88 respectively. This means that the phenolic compounds of the plants extracts contributed by 77% and 78% to their antioxidant and α-glucosidase inhibition activities respectively.

The positive correlations between phenolic compounds and antioxidant activities in our study are similar to the results of previous studies [30]. Strong correlations were also observed between antioxidant activity and flavonoid compounds (71%, 69%) and α-glucosidase inhibition activity (72%). Due to the low correlation coefficients of βC, it cannot be said βC did not play an important role on antioxidant and α-glucosidase inhibition activities.

4. Conclusions

Overall, the plants of the present study were rich in total phenolics. Furthermore, all the extracts exhibited antioxidant activity and inhibitory potential against α-glucosidase *in vitro*. Therefore, the plants could be used as alternative source to synthetic antioxidants and drugs for treatment some disease due to their high biological activity. Further *in vivo* and *in vitro* studies are necessary to provide better knowledge to reveal more information on the mode of action mechanism how the endogenous antioxidant and phenolic compounds of these extracts may prevent oxidative damage.

Compliance with Ethics Requirements. Authors declare that they respect the journal's ethics requirements. Authors declare that they have no conflict of interest and all procedures involving human / or animal subjects (if exist) respect the specific regulation and standards. Authors declare that they present their own literature survey and results/discussion/conclusion in the article.

References

1. Schloesser, A.; Esatbeyoglu, T.; Schultheiss, G.; Vollert, H.; Luersen, K.; Fischer, A.; Rimbach, G., Antidiabetic Properties of an Apple/Kale Extract *In Vitro*, *In Situ*, and in Mice Fed a Western-Type Diet, *Journal of Medicinal Food* **2017**, *20*(9), 846-854, https://doi.org/10.1089/jmf.2017.0019.
2. Alnajjar, M.; Barik, S.K.; Bestwick, C.; Campbell, F.; Cruickshank, M.; Farquharson, F.; Holtrop, G.; Horgan, G.; Louis, P.; Moar, K.-M.; Russel, W.R.; Scobbie, L.; Hoggard, N., Anthocyanin-enriched bilberry extract attenuates glycaemic response in overweight volunteers without changes in insulin, *Journal of Functional Foods* **2020**, *64*, 103597, https://doi.org/10.1016/j.jff.2019.103597.
3. Chi, G.; Qi, Y.; Li, J.; Wang, L.; Hu, J., Polyoxomolybdates as alpha-glucosidase inhibitors: Kinetic and molecular modeling studies, *Journal of Inorganic Biochemistry* **2019**, *193*, 173-179.
4. Zhao, X.; Tao, J.; Zhang, T.; Jiang, S.; Wei, W.; Han, H.; Shao, Y.; Zhou, G.; Yue, H.; Resveratroloside alleviates postprandial hyperglycemia in diabetic mice by competitively inhibiting alpha-glucosidase, *Journal of Agricultural and Food Chemistry* **2019**, *67*(10), 2886-2893.
5. Sohretoglu, D.; Sari, S.; Barut, B.; Ozel, A.; Discovery of potent alpha-glucosidase inhibitor flavonols: Insights into mechanism of action through inhibition kinetics and docking simulations, *Bioorganic Chemistry* **2018**, *79*, 257-264.
6. Fujita, A.; Sarkar, D.; Wu, S.; Kennelly, E.; Shetty, K.; Genovese, M.I., Evaluation of phenolic-linked bioactives of camu-camu (Myrciaria dubia Mc. Vaugh) for antihyperglycemia, antihypertension, antimicrobial properties and cellular rejuvenation, *Food Research International* **2015**, *77*, 194–203.
7. Erel, S.B.; Demir, S.; Nalbantsoy, A.; Ballar, P.; Khan, S.; Yavasoglu, N.U.K.; Karaalp, C., Bioactivity screening of five *Centaurea* species and in vivo anti-inflammatory activity of *C. Athoa*, *Pharmaceutical Biology* **2014**, *52*(6), 775-781.
8. Koc, S.; Isgor, B.S.; Isgor, Y.G.; Moghaddam, N.S.; Yıldırım, O., The potential medicinal value of plants from asteraceae family with antioxidant defence enzymes as biological targets, *Pharmaceutical Biology* **2015**, *53*, 746-751.
9. Zengin, G.; Zheleva-Dimitrova, D.; Gevrenova, R.; Nedialkov, P.; Mocan, A.; Ciric, A., Glamoclija, J.; Sokovic, M.; Aktumsek, A.; Mahomoodally, M.F., Identification of phenolic components via LC–MS analysis and biological activities of two *Centaurea* species: *C. drabifolia* subsp. *drabifolia* and *C. Lycopifolia*, *Journal of Pharmaceutical and Biomedical Analysis* **2018**, *149*, 436-441.
10. Lockowandt, L.; Pinela, J.; Roriz, C.L.; Pereira, C.; Abreu, R.M.V.; Calhelha, R.C.; Alves, M.J.; Barros, L.; Bredol, M.; Ferreira, I,C., Chemical features and bioactivities of cornflower (Centaurea cyanus L.) capitula: the blue flowers and the unexplored non-edible part, *Industrial Crops and Products* **2019**, *128*, 496-503.
11. Singleton, V.L.; Orthofer, R.; Lamuela-Raventós, R.M., Analysis of total phenols and other oxidation substrates and antioxidants by means of Folin-Ciocalteu reagent, *Methods in Enzymology* **1998**, *299*, 152–178.
12. Zhishen, J.; Mengcheng, T.; Jianming, W., The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals, *Food Chemistry* **1999**, *64*, 555–559.
13. Singh, R.P.; Murthy, K.N.C.; Jayaprakasha, G.K., Studies on the antioxidant activity of pomegranate (*Punica granatum*) peel and seed extracts using in vitro models, *Journal of Agricultural and Food Chemistry* **2002**, *50*, 81-86.
14. Re, R.; Pellegrini, N.; Protrggente, A.; Pannala, A.; Yang, M.; Rice-Evans, C., Antioxidant activity applying an improved ABTS radical cation decolorization assay, *Free Radical Biology and Medicine* **1999**, *26*, 1231-1237.
15. Mcdougall, G.J.; Shpiro, F.; Dobson, P.; Smith, P.; Blake, A.; Stewart, D., Different polyphenolic components of soft fruits inhibit α-amylase and α-glycosidase, *Journal of Agricultural and Food Chemistry* **2005**, *53*, 2760–2766.
16. McDougall, G.J.; Kulkarni, N.N.; Stewart, D., Berry polyphenols inhibit pancreatic lipase activity in vitro, *Food Chemistry* **2009**, *115*, 193–199.
17. Mahdavikia, F.; Saharkhiz, M.J.; Karami, A., Defensive response of radish seedlings to the oxidative stress arising from phenolic compounds in the extract of peppermint (*Mentha× piperita L.*), *Scientia Horticulturae* **2017**, **214**, 133-140.
18. Pérez, M.G.F.; Rocha-Guzmán, N.E.; Mercado-Silva, E.; Loarca-Piña, G.; Reynoso-Camacho, R., Effect of chemical elicitors on peppermint (*Mentha piperita*) plants and their impact on the metabolite profile and antioxidant capacity of resulting infusions, *Food chemistry* **2014**, *156*, 273-278.
19. Yi, W.; Wetzstein, H.Y., Biochemical, biological and histological evaluation of some culinary and medicinal herbs grown under greenhouse and field conditions, *Journal of the Science of Food and Agriculture* **2010**, *90*, 1063–1070.
20. Karadağ, A., 'Türkiye'deki Bazı Tıbbi ve Aromatik Bitkilerin Antioksidan Potansiyelleri ve Fenolik Kompozisyonları', *European Journal of Science and Technology* **2019**, *16*, 631–637.

21. Albayrak, S.; Aksoy, A.; Albayrak, S.; Sagdic, O., *In vitro* antioxidant and antimicrobial activity of some Lamiaceae species, *Iranian Journal of Science & Technology* **2013**, *A1*, 1-9.
22. Zengin, G.; Llorent-Martínez, E.J.; Córdova, M.L.F.; Bahadori, M.B.; Mocan, A.; Locatelli, M. Aktumsek, A., Chemical composition and biological activities of extracts from three *Salvia* species: *S. Blepharochlaena*, *S. Euphratica* var. *leiocalycina*, and *S. Verticillata* subsp. *amasiaca*, *Industrial Crops and Products* **2018**, *111*, 11–21.
23. Çam, M.; Başyiğit, B.; Alaşalvar, H.; Yılmaztekin, M.; Ahhmed, A.; Sağdıç, O.; Telci, İ.; Konca, Y., Bioactive properties of powdered peppermint and spearmint extracts inhibition of key enzymes linked to hypertension and type 2 diabetes, *Food Bioscience* **2020**, *35*,100577–0.
24. Pavlić, B.; Teslić, N.; Zengin, G.; Đurović, S.; Rakić, D.; Cvetanović, A.; Gunes, A.K.; Zeković, Z., Antioxidant and enzyme-inhibitory activity of peppermint extracts and essential oils obtained by conventional and emerging extraction techniques, *Food Chemistry* **2021**, *338*, 127724.
25. Ercan, P.; El, S.N., Bioaccessibility and inhibitory effects on digestive enzymes of carnosic acid in sage and rosemary, *International Journal of Biological Macromolecules* **2018**, *115*, 933–939.
26. Gonçalves, S.; Moreira, E.; Grosso, C.; Andrade, P.B.; Valentão, P.; Romano, A., Phenolic profile, antioxidant activity and enzyme inhibitory activities of extracts from aromatic plants used in Mediterranean diet, *Journal of Food Science and Technology* **2017**, *54*, 219–227.
27. Costamagna, M.S.; Zampini, I.C.; Alberto, M.R.; Cuello, S.; Torres, S.; Pérez, J.; Quispe, C.; Schmeda-Hirschmann, G.; Isla, M.I., Polyphenols rich fraction from Geoffroea decorticans fruits flour affects key enzymes involved in metabolic syndrome, oxidative stress and inflammatory process, *Food Chemistry* **2016**, *190*, 392–402.
28. Pradeep, P.M.; Sreerama, Y.N., Impact of processing on the phenolic profiles of small millets: evaluation of their antioxidant and enzyme inhibitory properties associated with hyperglycemia, *Food Chemistry* **2015**, *169*, 455–463.
29. Rajan, L.; Palaniswamy, D.; Mohankumar, S.K., Targeting obesity with plant-derived pancreatic lipase inhibitors: A comprehensive review, *Pharmacological Research* **2020**, *155*, 104681.
30. Başyiğit, B.; Çam, M.; Akyurt, B., Phenolıc compounds content antioxidant and antidiabetic potentials of seven edible leaves, *Gıda* **2018**, *43*(5), 876–885.