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HPTLC quantification, assessment of antioxidant potential and *in vivo* hypoglycemic activity of *Scorzonera latifolia* (Fisch. & C.A. Mey.) DC. and its major compounds

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ABSTRACT

Scorzonera L. (Asteraceae) species have long been the topic of many phytochemical, analytical, and biological studies since various species of the *Scorzonera* genus have been widely used as food and medicinal purposes. Apart from its traditional use to relieve pain, promote wound healing, treat helminth infections or women infertility, *Scorzonera latifolia* (Fisch. & Mey.) DC is also used for its antidiabetic activity. We aimed to investigate antidiabetic activity of the aerial parts of the title plant and its major secondary metabolites (hyperoside, isoquercitrin, 7-*O*-methylisoorientin, isoorientin, swertisin, chlorogenic acid, 4,5-*O*-dicaffeoylquinic acid and hydrangenol-8-*O*-β-glucoside) isolated from aerial parts in alloxan-induced diabetic mice. Blood glucose levels were measured four times: before the treatment, after 1st, 2nd, and 4th hours of sample treatments (100 mg/kg i.p.). *S. latifolia* extract displayed notable decline after 4 hours of administration. Among the metabolites; swertisin, 7-*O*-methyl-isoorientin, and hydrangenol-8-*O*-β-glucoside were associated with significant reduction on blood glucose level of alloxan-induced diabetic mice. Due to the strong relationship between oxidative stress and diabetes, antioxidant activity of *S. latifolia* was additionally tested. Furthermore, 4,5-*O*-dicaffeoylquinic acid, chlorogenic acid, hyperoside, and swertisin contents as major components of the extract were quantified by HPTLC-densitometry, as their biological effects can be attributed to their phenolic contents.

1. Introduction

Diabetes is characterized by inability of pancreas cells to produce any or adequate insulin, or inability of the body to utilize produced insulin (American Diabetes Association, 2015). If hyperglycemia is left uncontrolled, diabetes may cause fatal or debilitating macrovascular or microvascular consequences including myocardial infarction, stroke, retinopathy, nephropathy, etc. (Marles and Farnsworth, 1995). Numerous pathways where oxidative stress plays an important role have been accused by development of diabetic complications. The involvement of hyperglycemia-induced oxidative damage in diabetes may suggest that drugs which improve glycemic index and/or oxidative stress may be useful to manage the disease and its complications (Oyenihi et al., 2014; Sarian et al., 2017)

The genus *Scorzonera* (Asteraceae) is distributed mainly in the Asia, Europe, and Africa and represented with about 160 species (Coşkunçelebi et al., 2015). Several species of the *Scorzonera* genus have been commonly used as food and medicinal purposes (Bahadir et al., 2010). *Scorzonera latifolia* (Fisch. & C.A.Mey.) DC. occurs naturally in Turkey in Eastern Anatolia, northeastern Iran, and Caucasus and has characteristic green, entire, sparsely villous to glabrous leaves (Chamberlain, 1975). Previous studies reported its antioxidant, analgesic, anti-inflammatory, hepatoprotective, and anthelmintic properties (Bahadir et al., 2010, 2012; Bahadır-Acıkara et al., 2017; Baytop, 1999; Küpeli Akkol et al., 2011; Özbek et al., 2017). In addition, *Scorzonera* species were also reported to have ethnobotanical importance for their antidiabetic activities (Baytop, 1999; Cakilcioglu and Turkoglu, 2010; Dalar, 2018; Polat et al., 2013). Previous studies have shown that *Scorzonera* species contain flavonoids, phenolic acids including caffeoylquinic acid derivatives (Sari, 2012; Tsevegsuren et al., 2007; Wang et al., 2012; Zhu et al., 2009),

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dihydroisocoumarins (Saltan Çitoğlu et al., 2010), benzyl phthalides, stilbenoids, phenylbenzofuran derivatives (Sari, 2012; Sarı, 2010; Zidorn et al., 2000b), sesquiterpenoids such as bisabolene (Zidorn et al., 2000a), guaianolide derivatives (Granica et al., 2015; Tsevegsuren et al., 2007; Zhu et al., 2010, 2009; Zidorn et al., 2000a), and triterpenoids (Bahadır-Acıkara et al., 2018; Bahadır Acıkara et al., 2012).

In this study, we investigated *S. latifolia* extract and its major metabolites which were previously isolated [chlorogenic acid (**1**), 4,5-*O*-dicaffeoylquinic acid (**2**), hyperoside (**3**), isoquercitrin (**4**), isoorientin (**5**), 7-*O*-methylisoorientin (**6**), swertisin (**7**), hydrangenol-8-*O*-β-glucoside (**8**)] (**Figure 1**) for their potential hypoglycemic activities using alloxan-induced test model (Bahadır-Acıkara et al., 2017). Considering the relationship between DM and oxidative stress (Piconi et al., 2003), we also examined the antioxidant activity of the extract for further evaluation. Moreover, we also quantified the compounds, which were previously detected in significant amounts in *Scorzonera* sp. (Bahadır-Acıkara et al., 2017; Küpeli Akkol et al., 2011; Lendzion et al., 2021) along with marked antioxidant and antidiabetic activities (Gao et al., 2019; Xu et al., 2012), in the extract by HPTLC-densitometry.

2. Materials and method

2.1. Plant material

S. latifolia (Fisch. & C.A.Mey.) DC was collected from Bayburt, Kop Passage Turkey. The taxonomic identification of the plants was conducted in an independent qualified laboratory by Prof. Hayri Duman who is a plant taxonomist in Gazi University. The shade-dried upper

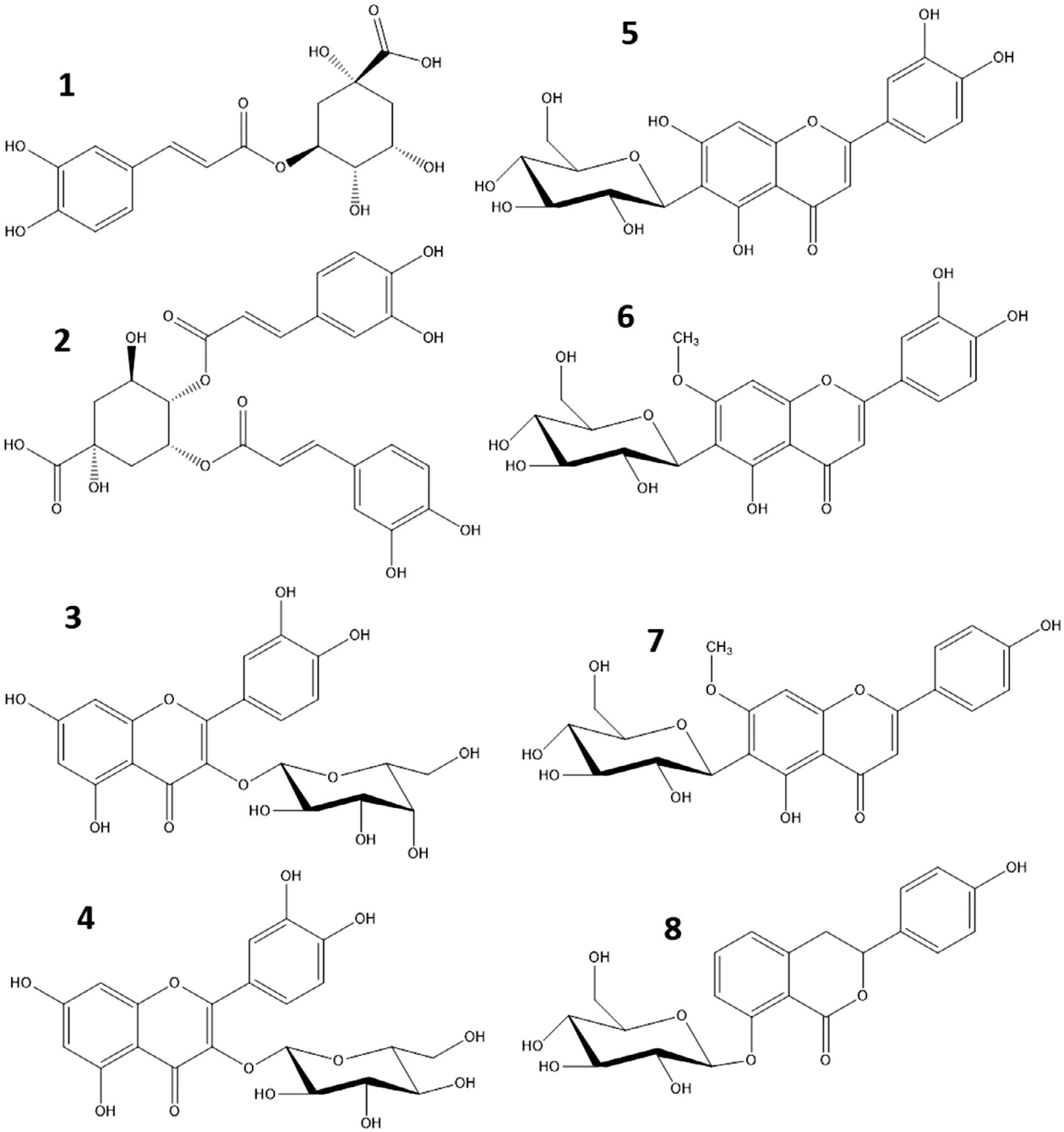

Fig.1. Molecular structures of the compounds.

ground parts of plant samples were kept at room temperature till the further use in air-tight containers. Voucher specimens are saved in the herbarium of Faculty of Pharmacy, Ankara University (Herbarium Number: AEF 23827).

2.2. Preparation of the extract

Powdered and dried aerial parts (20 g) of the plant material were extracted with water: methanol mixture (20:80, 100 ml) at room temperature by continuous stirring for 8 hours for 3 days. With the help of a rotary evaporator, the extract was concentrated and filtered to dryness under reduced pressure and low temperature (40–50°C) to yield crude extract (extract amount 6.418 g). Chlorogenic acid, 4,5-*O*-dicaffeoylquinic acid, hyperoside, isoquercitrin, isoorientin, 7-*O*-methylisoorientin, swertisin, and hydrangenol-8-*O*-β-glucoside were isolated over again from *S. latifolia* aerial parts from ethyl acetate fraction of the methanolic extract, as described previously (Bahadır-Acıkara et al., 2017).

2.3. Animals

The study protocol was approved by Istanbul Medipol University Animal Experiments Ethics Committee (01/02/2017-03, 31/08/2018-53). Female Balb/C strain mice (22-30 g) were used to examine antidiabetic activity. The animals were housed at room temperature (22 ± 2°C) in standard cages (48 cm x 35 cm x 22 cm) with artificial light from 7.00 am to 7.00 pm and provided with pelleted food and water ad libitum.

2.4. Antidiabetic activity assay

Antidiabetic activity was evaluated with an alloxan-induced test model (Ozbek et al., 2017; Tripathi and Verma, 2014). Mice were starved food before the alloxan treatment for 18 hours. Alloxan applied in an isotonic saline solution (ISS) by intraperitoneal administration (i.p.) (150 mg/kg) three times in a 48-hour period. After 10 days from alloxan treatment procedure, mice were starved 18 hours and blood glucose levels were measured with an Accu-Check® sugar strip. Mice with blood glucose levels of 200 mg/dL and higher were grouped as diabetic animals. Animals were divided into the following groups (n=5): Group 1, the control group, received ISS 0.1 mL, and the other groups received *S. latifolia* extract 100 mg/kg i.p. This procedure was followed by an isolated compound investigation to determine the antidiabetic activities of compounds (all compounds were dissolved in an isotonic saline solution). Animals were assigned one of the eight groups (n=5) that received chlorogenic acid, 4,5-*O*-dicaffeoylquinic acid, hyperoside, isoquercitrin, isoorientin, 7-*O*-methylisoorientin, swertisin, or hydrangenol-8-*O*-β-glucoside 100 mg/kg i.p.

Following the administration of *S. latifolia* extract and the compounds, blood samples were collected in the 1st, 2nd and 4th hours and measured for their glucose concentrations. This was performed via sugar strips that use the glucose-oxidase-peroxidase method.

2.5. Antioxidant activity determination

2.5.1. Diphenylpicrylhydrazyl (DPPH) radical-scavenging activity

The plant extract was diluted with H_2O and mixed with 100 μM DPPH solution dissolved in methanol. The mixture was kept at room temperature and in the dark and then the decrement in the absorption was investigated at 517 nm. Butylated hydroxytoluene was selected as the reference compound.

2.5.2. Cupric reducing antioxidant capacity (CUPRAC)

The CUPRAC of the extract was determined by the assay adapted before (Bardakci et al., 2020). Copper (II) sulfate and neocuproine was added in the ammonium acetate buffer in equal volume. Following the mixing, the extract was added to the mixture and kept at room temperature for one hour. Afterwards, the absorbance of the mixture was measured via UV spectrometer at 450 nm. The results were calculated as milligram ascorbic acid equivalent per g DE.

2.5.3. Ferric reducing antioxidant power (FRAP)

FRAP activity was assessed via spectrophotometric method using the previously described assay (Barak et al., 2019). Accordingly, the plant extract was mixed with freshly prepared FRAP solution and the final volume was set to 0.3 mL. After 30 min of incubation, the absorbance was retrieved at 593 nm. Butylated hydroxytoluene was selected as the reference compound. The results were calculated as mM $FeSO_4$ per g DE.

2.5.4. Determination of total antioxidant capacity by phosphomolybdenum method

Total antioxidant capacity was calculated by a method using reduction of phosphomolybdenum which was adapted in a previous study (Barak et al., 2019). A mixture was freshly prepared for the reaction that contained H_2SO_4, sodium phosphate monobasic, and ammonium molybdate. Sufficient amount of plant extract was added to the mixture before the incubation period in a water bath at 95°C for 90 min at dark. After the incubation, the absorbance was determined at 695 nm. Results were given as mg ascorbic acid equivalent per g DE.

2.6. Quantification of 4,5-O-dicaffeoylquinic acid, chlorogenic acid, hyperoside, and swertisin by HPTLC

4,5-*O*-dicaffeoylquinic acid, chlorogenic acid, hyperoside, and swertisin contents were determined by using a method published previously (Creţu et al., 2013). The standard solutions of 4,5-*O*-dicaffeoylquinic acid, chlorogenic acid, hyperoside, and swertisin (50 μg/mL) were prepared in MeOH, and 500 mg of total extract and each fraction were dissolved in 10 mL MeOH (5 mg/mL extract). Each sample was filtered through a 0.45 μm syringe filter. Adequate amount of plant extract and at least five different concentrations of standard compounds were applied in triplicate. The bands containing sample and standard solutions were inoculated with the length of 8 mm on silica gel glass HPTLC plates 60 F_{254} with Camag Automatic TLC Sampler IV. A constant application rate was applied and the spaces between the tracks were set to 10 mm. The mixture of ethyl acetate (EtOAc):acetic acid (AA):formic acid (FA):H_2O 10:1.1:1.1:2.3 (v/v/v/v) was used as the mobile phase. Camag Automatic Developing Chamber (ADC-2) was used to carry out the development. Saturation was done in the chamber for 20 min and the plate was preconditioned for 5 min prior the development. Controlled humidity was established by ADC-2 using $MgCl_2$ (33% RH) for 10 min. Densitometric screening was performed by using Camag TLC Scanner IV and VisionCATS software in fluorescence mode. The slit dimension was kept at 5 × 0.2 mm, micro and the scanning speed was set at 20 mm/s. Standard contents were afforded by comparing AUCs with the calibration curve of standards. The coefficient of variation (CV%) is under 1.00 and the correlation coefficient (R) of the calibration curve was above 0.998. The presence of standards in extracts was defined by evaluation of both retention factors (R*f*) and overlaying UV spectra of each extract and standards.

2.7. Statistical analyses

Statistical analysis was performed by using SPSS 24.0 software. Data were expressed as mean ± standard error of mean (SEM). A one-way analysis of variance (post-hoc Dunnett-t test) was carried out for analyses. An overall type I error of 5% was used to infer statistical significance.

Table 1
Blood glucose level of *Scorzonera latifolia* and its' major compounds in alloxan-induced diabetic mice.

Groups	Blood glucose levels (mg/dL)			
	Before treatment	After treatment		
		Hour 1	Hour 2	Hour 4
Control (isotonic saline solution)	470.6±23.6	472.2±13.94	493.8±15.6	494.2±27.3
S. latifolia	457.6±31.5	360.6±66.8	308.4±68.4	249.0±71.6*
Chlorogenic acid	289.2±28.4	381.0±24.4	329.2±15.9	286.6±14.6
4,5-*O*-dicaffeoylquinic acid	382.8±41.8	455.4±47.3	430.2±65.6	358.2±72.6
Hyperoside	442.6±54.2	485.4±32.4	437.6±36.5	392.0±61.6
Isoquercitrin	457.6±18.3	503.2±22.2	474.2±14.4	345.8±75.1
7-*O*-methylisoorientin	377.4±71.3	322.0±73.7	282.2±82.1*	253.6±88.3*
Swertisin	363.6±48.0	395.8±35.0	237.8±58.6*	257.2±56.8*
Isoorientin	421.4±47.9	445.4±75.6	410.6±67.0	381.0±57.0
Hydrangenol-8-*O*-β-glucoside	295.4±26.7	248.6±46.8*	217.4±51.6*	213.6±52.4*

*$p<0.05$; comparison with saline group.

3. Results

The mean blood glucose level of alloxan-induced diabetic mice were significantly lower after 4 hours of *S. latifolia* extract treatment (249.0 ± 71.6 mg/dL) compared to the mean ISS group at Hour 4 (494.2 ± 27.3 mg/dL, $p<0.05$). The reductions compared to that of the control group at Hour 1 or Hour 2 were not statistically significant. In terms of isolated compounds; hydrangenol-8-*O*-β-glucoside was associated with significantly lower blood glucose levels at Hour 1 (248.6 ± 46.8 mg/dL), Hour 2 (217.4 ±51.6 mg/dL) and Hour 4 (213.6 ± 52.4 mg/dL) compared to those of the ISS group ($p<0.05$ for each). Additionally, the mice receiving 7-*O*-methylisoorientin or swertisin had significantly lower blood glucose levels at both Hour 2 (282.2 ± 82.1 mg/dL and 237.8 ± 58.6 mg/dL, respectively) and Hour 4 (253.6 ± 88.3 mg/dL and 257.2 ± 56.8 mg/dL, respectively) compared to those of the control group (Table 1).

In vitro antioxidant activity levels were summarized in Table 2. When compared with the positive controls, the plant extract showed significant *in vitro* antioxidant capacity, as shown by all of the DPPH, FRAP, CUPRAC, and TOAC methods (Table 2).

4,5-*O*-dicaffeoylquinic acid, chlorogenic acid, hyperoside, and swertisin contents of the extracts were quantified by using HPTLC. The R*f* values were calculated as 0.825, 0.545, 0.668, and 0.679, respectively (Figure 2). The verifications of standard compounds in plant sample were proved by comparison of R*f* values as well as their overlapping UV spectra. HPTLC analysis demonstrated that among the tested major metabolites, *S. latifolia* extract was dominated by chlorogenic acid (5.63%) and hyperoside (3.82%). The results of HPTLC analysis was shown in Table 3.

Table 2
In vitro antioxidant activity of Scorzonera latifolia extract.

Extract	DPPH[a]	FRAP[b]	CUPRAC[c]	TOAC[c]
S. latifolia	673.5 ± 14.2	2.3 ± 0.1	402.3 ± 8.1	328.9 ± 10.7

1) EC_{50} value of the reference compound "butylated hydroxytoluene" in DPPH scavenging activity is found to be 415.26 ± 12.85 μg/ml 2) FRAP activity of the reference compound "butylated hydroxytoluene" is found to be 3.48 ± 0.18 mM $FeSO_4$ eq. in 1 g sample.
DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, ferric reducing antioxidant power; CUPRAC, cupric reducing antioxidant capacity; TOAC, total antioxidant capacity.
[a] Results were expressed as the mean of triplicates ± standard deviation and DPPH activity was expressed as EC_{50} in μg/ml equivalents.
[b] Results were expressed as the mean of triplicates ± standard deviation and as mM $FeSO_4$ equivalents in 1 g sample.
[c] Results were expressed as the mean of triplicates ± standard deviation and as mg ascorbic acid equivalents (AAE) in 1 g sample.

4. Discussion

DM is a fast-growing metabolic disease characterized by hyperglycemia, glycosuria, and hyperlipidemia (American Diabetes Association, 2015). Although insulin and other antidiabetic agents help to improve glycemic control in DM, new treatment options are still needed for this disease. There exist several studies that can be found related to Scorzonera spp. especially about its phytochemistry (Bahadır-Acıkara et al., 2017; Küpeli Akkol et al., 2011; Özbek et al., 2017; Sari, 2012). Nonetheless, none of the published research has explained the antidiabetic activity of *S. latifolia* including either chemistry or biological activity. This study establishes the first report on the simultaneous determination of antidiabetic and antioxidant activities of *S. latifolia* and its major phenolic metabolites as well as their quantification.

Among the variations of the methods used for the evaluation of the antioxidant activity, the DPPH test along with the metal-chelating assays as well as antioxidant capacity assay, are very useful in the micromolar range, requiring minutes to hours. Utilized *in vitro* assays assessing the antioxidant potential revealed that aqueous methanolic extract of *S. latifolia* aerial parts showed significant activity. The majority of the bioactivities of plants have been attributed to their polyphenol and flavonoid contents (Jebur et al., 2016; Marles and Farnsworth, 1995; Vinayagam and Xu, 2015). As *in vivo* antidiabetic activities of the extract and its isolates showed promising data, mechanisms of antioxidant and antidiabetic activity should be enlightened.

Antidiabetic properties of *Scorzonera* spp. have been reported in Turkish folk medicine (Baytop, 1999; Cakilcioglu and Turkoglu, 2010; Dalar, 2018; Polat et al., 2013). Our findings that proved blood glucose-lowering activity with *S. latifolia* extract seem to be consistent with the literature. This activity may be related to its high antioxidant capacity (Bahadır-Acıkara et al., 2017; Erden et al., 2013). Flavonoids are secondary metabolites and it is known that they protect the body against free radicals and other pro-oxidative compounds. Furthermore, their use can be beneficial in DM treatment and to reduce the risk of developing new onset diabetes (Jebur et al., 2016; Vinayagam and Xu, 2015). Among various mechanisms that may help in the management of patients with DM, flavonoids have been demonstrated to increase insulin secretion by regeneration of pancreatic β-cells and insulin-mediated glucose uptake by target cells (Vinayagam and Xu, 2015).

Hyperoside, isoquercitrin, 7-*O*-methylisoorientin, and swertisin are classified as flavonoids among the tested compounds. After 2 and 4 hours of treatment of swertisin (6-*C*-glycoside of methoxy apigenin) administration, blood glucose level became significantly diminished in the present study. Swertisin has a peculiar mechanism to achieve normoglycemic status in diabetic mice. Swertisin was reported to have excellent inhibitory effects on aldose reductase,

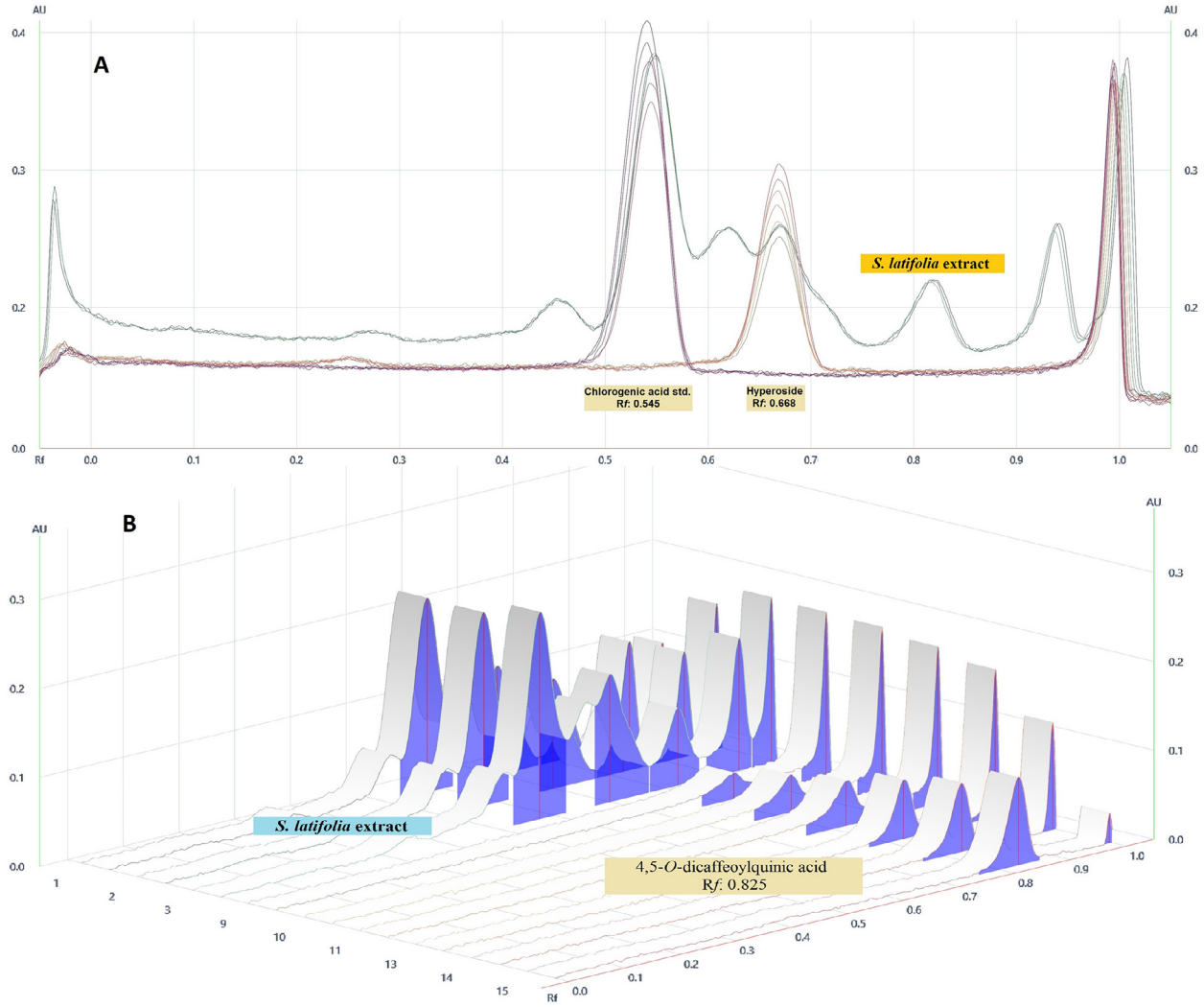

Fig. 2. A. HPTLC chromatogram of chlorogenic acid, hyperoside, and *S. latifolia* extract. **B.** HPTLC chromatogram of 4,5-*O*-dicaffeoylquinic acid, and *S. latifolia* extract.

which was associated with long-term diabetic complications, e.g., cataract. It was also reported to produce cytoprotective activity against streptozotocin and provide normoglycemic conditions 60 mins after a high dose of glucose administration, along with producing a considerable rise in the serum insulin level in rats (Patel and Mishra, 2011). Moreover, swertisin is an effective differentiating agent, providing islet-like cell types with enormous yield and mature functional status (Dadheech et al., 2013). Swertisin was also tested at molecular, immunological, and functional plane in order to confirm proper differentiation in ILCC (islet-like cell clusters). The hypoglycemic effect of transplanted ILCC was tested in diabetic mice, suggesting the integrity plus functional maturity of newly-generated ILCC. Swertisin treatment differentiated human and mouse pancreatic progenitor cells in insulin producing cells (Dadheech et al., 2015). Diabetic mice which were administered swertisin were reported to show reversion to normoglycemia and a considerable increase of fasting serum insulin levels. After swertisin treatment, pancreatic tissue of diabetic mice was reported to have a substantial up-regulation of key transcription factors required for islet neogenesis and beta cell homeostasis (Srivastava et al., 2018). Similar results were also obtained with isoorientin and 7-*O*-methylisoorientin. Isoorientin did not show significant activity while 7-*O*-methyl isoorientin resulted in a significant hypoglycemic activity after 2 and 4 hours of treatment. Isoorientin has been previously isolated as antidiabetic agent from *Gentiana olivieri* (Sezik et al., 2005). This does not seem to be supported by our findings as isoorientin treatment in our study induced only a slight and nonsignificant hypoglycemic activity in diabetic animals. On the other hand, 7-*O*-methyl isoorientin reduced blood glucose level significantly after 2 and 4 hours of treatment in the same conditions.

Hydrangenol-8-*O*-β-glucoside, an isocoumarin glycoside, was tested for its antidiabetic activity. A remarkable hypoglycemic

Table 3
Quantification data for 4,5-*O*-dicaffeoylquinic acid, chlorogenic acid, hyperoside, and swertisin from *S. latifolia* extract.

Extract	4,5-*O*-dicaffeoylquinic acid (w/w%)	CV %	Chlorogenic acid (w/w%)	CV %	Hyperoside (w/w%)	CV %	Swertisin (w/w%)	CV%
S. latifolia	1.702	0.19	5.63	0.96	3.82	0.22	0.8142	2.13

*CV: Coefficient of Variation

activity after 2 and 4 hours of treatment with a 100 mg/kg dosage of hydrangenol-8-*O*-β-glucoside was observed. Hydrangenol, an aglycone of hydrangenol-8-*O*-β-glucoside was reported to considerably lower blood glucose and free fatty acid levels (Matsuda et al., 2014). In addition, while having similar effects to troglitazone -a thiazolidinedione used in diabetes-, hydrangenol showed less agonistic activity for proliferator-activated receptor gamma2 (PPARγ2), unlike troglitazone. Other thiazolidinediones, pioglitazone and rosiglitazone are potent ligands of PPARγ, and therefore, these drugs are potent insulin sensitizers currently used in the management of type-2 diabetes. Thiazolidinedione-like compounds known as antihyperglycemic drugs, are also able to enhance other symptoms associated with type 2 diabetes, including hyperlipidemia, atherosclerosis, and chronic inflammation. In the same study, hydrangenol-8-*O*-β-glucoside displayed insignificant activity (Matsuda et al., 2014; Zhang et al., 2007).

Hyperoside, in type 2 diabetic rats, may have hypoglycemic activity by improving the function of pancreatic islets and enhancing glycolysis, and by reducing gluconeogenesis (Zhang et al., 2018). Furthermore, several studies have demonstrated that quercetin which is an aglycone of hyperoside, prevented and protected oxidative stress and β-cell damage in the rat pancreas while streptozotocin induction. These results suggest that hyperoside may protect the islet cells from injuries induced by oxidative stress (Zhang et al., 2018). Moreover, the administration of isoquercetin to diabetic animals was reported to lower serum glucose with a parallel increase in insulin levels, as well as the inhibition of the activity of hepatic glucose-6-phosphatase (Panda and Kar, 2007). While hyperoside and isoquercitrin were reported to exert miscellaneous activities on alloxan-induced diabetic mice, the reduction on blood glucose level at 1, 2, and 4 hours after treatment with either of these compounds was not statistically significant in our study.

Some earlier studies demonstrated that phenolic acids may be beneficial in DM and metabolic syndrome. In this study, chlorogenic acid and 4,5-*O*-dicaffeoylquinic acid were the phenolic acids that are isolated from *S. latifolia*. Chlorogenic acid is one of the most widely distributed phenolic acids in the plant kingdom and in the human diet in numerous fruits and vegetables as well as having a high concentration in coffee (Manach et al., 2004). Consumption of chlorogenic acid-rich coffee has been associated with a lower risk of type 2 DM (Ong et al., 2013). Moreover, the enzyme tyrosine phosphatase 1B catalyzes the hydrolysis of phosphotyrosine from specific proteins and regarded as a new target due to its negative regulatory effect on insulin-receptor and leptin-receptor signaling pathway. 4,5-*O*-dicaffeoylquinic acid was found to have an inhibitory effect on α-glucosidase and tyrosine phosphatase 1B (Chen et al., 2014; Verma et al., 2017). In the current study, we did not observe any remarkable activity on blood glucose levels after 1, 2 and 4 hours of treatment with 100 mg/kg dose of chlorogenic acid and 4,5-*O*-dicaffeoylquinic acid on alloxan-induced diabetic mice. These results may suggest that a longer treatment of phenolic acids is required in order to improve glucose and lipid metabolism disorders and to prevent diabetic complications (Jin et al., 2015).

In conclusion, the use of *S. latifolia* in Turkish folk medicine for glucose-lowering purposes has been demonstrated by this study as *S. latifolia* aerial part extract displayed hypoglycemic activity. Furthermore, swertisin, 7-*O*-methyl-isoorientin, and hydrangenol-8-*O*-β-glucoside seem to be promising for their potential hypoglycemic activities. Considering that *Scorzonera* spp. have the potential for their antidiabetic activity, further well-designed studies needs to be conducted to interpret their mechanism of action and uncover any possible association between antioxidant activity and hypoglycemic potential.

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Declaration of Competing Interest

The authors declared no conflict interest.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.sajb.2022.07.041.

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