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Phenolic Profile, Inhibition of α-Amylase and α-Glucosidase Enzymes, and Antioxidant Properties of *Solanum elaeagnifolium* Cav. (Solanaceae): In Vitro and In Silico Investigations

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Abstract: In this study, the chemical composition and the antioxidant and antidiabetic properties of *S. elaeagnifolium* flower (SEFl), fruit (SEFr), and leaf (SEFe) extracts were investigated in vitro and in silico. HPLC-DAD analysis was used to determine the chemical components. Colorimetric techniques were used to identify polyphenols and flavonoids. The antioxidant capacity was determined using DPPH and TAC assays. The antidiabetic activity was examined using the enzymes α-amylase and α-glucosidase. Molecular docking methods were used to assess the anti-dipeptidyl peptidase IV (DPP-IV) activity. According to HPLC findings, extracts of *S. elaeagnifolium* flowers, leaves, and fruits are rich in salicylic acid, sinapic acid, chlorogenic acid, naringin, quercetin, quercetin-3-O-beta-glucoside, kaempferol, and chalcone. The IC_{50} for flower, leaf, and fruit extracts were 132 ± 5.59 µg/mL, 43.19 ± 1.46 µg/mL, and 132 ± 5.59 µg/mL, respectively. The total antioxidant capacity of SEFr, SEFe, and SEFl were determined to be 900.06 ± 4.01 µg AAE/mg, 792.10 ± 6.72 µg AAE/mg, and 681.10 ± 3.02 µg AAE/mg, respectively. Importantly, SEFe, SEFl, and SEFr displayed significant anti-α-amylase activity, with IC_{50} values of 79.16 ± 2.35 µg/mL, 99.16 ± 1.17 µg/mL, and 40.31 ± 2.04 µg/mL, respectively. The results also showed that SEFr, SEFe, and SEFl all exhibited potent anti-α-glucosidase activity, whose IC_{50} values were determined to be 20.53 ± 0.37 µg/mL (SEFr), 20.05 ± 0.12 µg/mL (SEFe), and 41.1 ± 1.55 µg/mL (SEFl). Molecular docking of *S. elaeagnifolium* phenolic compounds in the active site of DPP-IV revealed a strong inhibitory effect, with a glide score ranging from −2.63 to −8.10 Kcal/mol. Notably—with glide scores of −8.10, −6.23, −5.73, and −5.37 Kcal/mol—rutin, quercetin-3-O-beta-glucoside, chalcone, and naringin were the most active molecules against DPP-IV.

Keywords: *Solanum elaeagnifolium*; α-amylase; antioxidant; DPP-IV; α-glucosidase; HPLC-DAD

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1. Introduction

Diabetes mellitus (DM) is a multifaceted and complex public health problem, with a growing social and economic impact that has reached alarming epidemic proportions [1]. Diabetes has a higher incidence in Morocco compared to any other country in the world. According to research findings, the prevalence of type 2 diabetes among Moroccan adults, aged 20 and up, ranged from 6.6% in 2000 to 12.4% in 2016. Half of Moroccan diabetics are uninformed about their condition and the serious consequences it can have [2,3].

Type 2 DM is a carbohydrate metabolic condition characterized by insulin secretion defects caused by pancreatic beta cell dysfunction. Worldwide, approximately 90% of diabetic patients are non-insulin-dependent (type 2 diabetes) [4]. Being overweight is one risk factor for possible complications, including heart attack, kidney failure, stroke, vision loss, leg amputation, and loss of feeling. In addition, moderate to severe diabetes increases the risk of fetal death and other reproductive complications [5–7].

Carbohydrate enzymatic digestion and absorption by the intestinal mucosa play a role in postprandial blood glucose regulation. This role was considered in the diabetes therapy strategy, both in the advancement of nutritional advice and in the mechanism of action of oral antidiabetic drugs, which are focused on the action of α-glucosidase, α-amylase, and intestinal glucose transport [8].

Due to the toxicity and side effects of some current antihyperglycemic drugs, researchers have been searching for new naturally occurring inhibitors of pancreatic α-amylase and intestinal α-glucosidase, particularly plants that have a hypoglycemic effect with few side effects. Diabetes has been managed using a variety of plants that intervene as enzyme inhibitors [6,7,9–13]. Diabetic populations around the world use various plants for their hypoglycemic properties, based on historical, cultural, and economic considerations. Plants have also long been used to treat chronic diseases, such as diabetes and hypertension [14,15].

Several pathologies, including arthritis, asthma, cancer, and diabetes, are thought to be caused by free radicals [16]. Free radicals are responsible for the oxidation of the body's constituents. This oxidation denatures proteins, lipids, sugars, DNA, as well as the body's cell membranes. This attack on cells is one of the primary causes of aging and is involved in a wide range of pathologies. The pancreatic cells responsible for insulin production are among the first to be affected by the negative effects of oxidative stress [17]. Using natural products (such as fruits and vegetables) that are high in antioxidants could help prevent these diseases. Furthermore, the high cost of health services and medicines, as well as socio-economic factors, drive a large portion of the population to seek medical treatment from medicinal plants. Currently, 80% of the population has used herbal medicine at some point [18]. Plant extracts are a rich source of antioxidants, particularly polyphenols, which include a wide range of compounds, such as flavonoids, anthocyanins, and tannins. These are widely distributed compounds found in plants. Indeed, by reducing hydroxyl and superoxide radicals, they are capable of scavenging free radicals and inhibiting lipid peroxidation [19].

Solanaceae is a plant family in the order of Solanales. It contains herbaceous plants, trees, shrubs, and vines that are widely distributed in both hemispheres' tropical regions, with a strong presence in South America, and a lower presence in temperate regions. This family contains approximately 147 genera and approximately 2930 species, with majority of these members being toxic due to the presence of tropanic and steroidal alkaloids. Plants such as *S. elaeagnifolium, S. trilobatum,* and *S. virginianum* are widely used in pharmaceuticals [20].

Solanum elaeagnifolium is an invasive species that grows in tropical and subtropical climates, and can be found at elevations higher than 1000 m. *S. elaeagnifolium* can grow in a variety of soil textures [21], and has analgesic, anti-inflammatory, antioxidant, insecticidal, molluscicidal, larvicidal, antimicrobial, chemopreventive, and antitumor properties [22–27]. Some of the major compounds in this plant, such as quercetin, gallic acid, kaempferol, and naringenin, are responsible for these activities [22,28,29].

The beneficial effects of the *Solanum* species on human and animal health are related to their high levels of flavonoids, alkaloids, terpenes, saponins, phenols, carotenoids, and coumarins [30,31]. Anticancer, antidepressant, anti-inflammatory, antihypertensive, antioxidant, hypolipidaemic, hypoglycemic, anti-obesogenic, hepatoprotective, and antidiabetic activities have been reported in some species [30,32–34].

In this new study, the composition of extracts from different parts of *S. elaeagnifolium* were analyzed by HPLC-DAD, and their in vitro and in silico antidiabetic and antioxidant potentials were evaluated.

2. Materials and Methods

2.1. Plant Extracts

S. elaeagnifolium (Voucher: E17/1405) (Figure 1) was collected in the Moroccan city of Fez in early December 2022. Next, the aerial parts—leaves (SEFe), flowers (SEFl), and fruits (SEFr)—were cleaned and dried before being ground. Maceration was employed to produce a hydroethanolic extract of the leaves, fruits, and flowers of *S. elaeagnifolium*. Notably, 50 g of plant powder was mixed with 500 mL of hydroethanolic solution (70% ethanol and 30% water). Subsequently, the mixture was macerated for 48 h at 24 ± 1 °C before being filtered through Whatman paper. Finally, the extracted samples were kept at 4 °C [35].

(**A**) (**B**) (**C**)

Figure 1. *S. elaeagnifolium* aerial parts (**A**), *S. elaeagnifolium* fruits (**B**), and *S. elaeagnifolium* flowers (**C**).

2.2. HPLC-DAD Analysis

Extracts of the different plant parts (SEFr, SEFl, and SEFe) were prepared at 50 mg/mL and filtered through microfilters (0.45 µm). Characterization of phenolic compounds was assessed using high-performance liquid chromatography HPLC, connected to a UV detector (210–400 nm). Notably, 40 µL was injected through a (C18) reverse phase column (250 × 4 mm, 5 µm) using an elution gradient at a 1 mL/min flow rate. The compounds were identified, as detailed in previous works [9,10,36].

2.3. Antioxidant Activity Assay

2.3.1. DPPH Assay

In brief, 50 µL of plant extract test samples of various concentrations were mixed with 50 µL of a DPPH solution (0.2 mM in methanol). Butylated hydroxytoluene (BHT) was used as a standard. After 30 min of incubation in the dark, the absorbance was measured using a UV-visible spectrophotometer at 517 nm. Calculations were performed based on Equation (1) and the results are reported as a percentage of inhibition [37,38]:

$$\text{P.I. } (\%) = \frac{\text{Abc} - \text{Abs}}{\text{Abc}} \times 100 \quad (1)$$

where Abc is the uptake of the negative control, and Abs is the uptake of the extract or standard.

2.3.2. TAC Assay

Total antioxidant capacity (TAC) was calculated as follows: 200 µL of a known concentration was mixed with 2 mL of reagent solution—0.6 mol/L sulfuric acid (H_2SO_4), 28 mmol/L sodium phosphate (Na_2PO_4), and 4 mmol/L ammonium molybdate ($(NH_4)_2MoS_4$)—then the mixture was cooled to room temperature (25 ± 1 °C) after being incubated at 95 °C for 90 min. Butylated hydroxytoluene (BHT) was used as a standard. The absorbance was calculated using 695 nm. The amount of equivalent ascorbic acid per gram of extract (mg EAA/g extract) was used to calculate the overall antioxidant activity [39–41].

2.4. Antidiabetic Activity Assay

2.4.1. α-Amylase Inhibition Assay

The method described by Hbika et al. [9] was used to test the inhibitory effect of *S. elaeagnifolium* on the enzymatic activity of α-amylase. A volume of 200 µL of α-amylase enzyme solution (obtained from Sigma Aldrich, St. Louis, MO, USA) was mixed with 200 µL of phosphate buffer solution and 10 µL of *S. elaeagnifolium* extract—or with the acarbose solution (positive control)—in each tube except the blank, where the enzyme solution was replaced by phosphate buffer (50 mM; pH = 7.5). The tubes were pre-incubated at 37 °C for 10 min. To block the enzymatic reaction, 600 µL of a colored DNSA reagent was added to the mixture, after which the tubes were immersed in a bubble bath for 8 min. This reaction was then halted by way of heat shock, which was achieved by immersing the tubes in a cold-water bath before adding 1 mL of distilled water to each tube. A spectrophotometer was used to measure the absorbance at 540 nm against a blank background containing the buffer solution, rather than the enzyme solution. The percentage inhibition of each extract, or acarbose, was calculated using Equation (1).

2.4.2. α-Glucosidase Inhibition Assay

Using a protocol developed by Loukili et al. [10], the effect of *S. elaeagnifolium* extracts on intestinal α-glucosidase activity was calculated by measuring the glucose released by sucrose degradation. Briefly, 100 µL of sucrose (50 mM), 1000 µL of phosphate buffer (50 mM; pH = 7.5), and 100 µL of α-glycosidase enzyme solution (obtained from Sigma Aldrich, St. Louis, MO, USA) were used as test solutions (10 I.U.). The previous mixtures were then treated with either 10 µL of the control (distilled water), positive control (acarbose), or *S. elaeagnifolium* extract solutions of various concentrations. The mixtures were then incubated in a 37 °C water bath for 25 min. The solution was heated to 100 °C for 5 min to stop the enzyme reaction, and the final solution's absorbance was measured at 500 nm. The calculations were performed based on Equation (1).

2.5. In Silico Studies

In this study, the antidiabetic activity against dipeptidyl peptidase IV (DPP-IV) was evaluated using molecular docking methods [42]. The phenolic compounds found in *S. elaeagnifolium* were retrieved from the PubChem database in SDF format and processed using the LigPrep tool in the Maestro 11.5 version of the Schrödinger Software program with the OPLS3 force field. Up to 32 stereoisomers were generated for each ligand after considering ionization states at pH 7.0 ± 2.0 [43].

The crystal structure of DPP-IV was obtained from the protein data bank in PDB format using the PDB IDs 1RIP. This structure was then prepared and refined using the Protein Preparation Wizard of Schrödinger-Maestro v11.5. The minimization of the structure was carried out using the OPLS3 force field [44]. The receptor grid was positioned at the following coordinates: X = 62.54, Y = 52.76, and Z = 85.31. A volumetric spacing of 20 × 20 × 20 was used. Flexible ligand docking was performed using the SP method in the Glide of Schrödinger-Maestro v11.5.2.5 [45].

2.6. Statistical Analysis

The results of this study were expressed as mean standard error (SEM). One-way ANOVA was used to analyze the data, followed by the Tukey post-test. Significant values are those with $p < 0.05$. GraphPad Prism 8.0.1 from GraphPad Software Inc., San Diego, CA, USA was used to analyze the data statistically.

3. Results and Discussion

3.1. HPLC Analysis

The chemical constituents of *S. elaeagnifolium* extracts were explored using liquid chromatography with high performance, coupled to a diode array detector (HPLC-DAD). Notably, Figure 2 illustrates the HPLC chromatograms of the identified polyphenols, while Table 1 illustrates the retention time and percentage area of the compounds in SEFr, SEFl, and SEFe. HPLC analysis demonstrated the presence of salicylic acid, ferulic acid, sinapic acid, cinnamic acid, chlorogenic acid, and rutin in SEFr. Salicylic acid, sinapic acid, naringin, quercetin, chlorogenic acid, quercetin-3-O-beta-glucoside, kaempferol, and chalcone were found to be prevalent in SEFe. Lastly, SEFl contained ferulic acid, sinapic acid, chlorogenic acid, quercetin, rutin, quercetin-3-O-beta-glucoside, and kaempferol. These findings are in agreement with previous research on the composition of the *Solanum* genus, which was found to be rich in phenols, such as chlorogenic acid, naringenin, and quercetin [22–24,28]. Plant parts, relative humidity, climatic conditions, soil, and post-harvest treatments can all influence chemical composition, as reported in earlier works [10,46,47]. Chromatographic analysis revealed the presence of chlorogenic acid and sinapic acid in the various extracts studied from the plant. Research has shown that these two compounds possess several biological activities, such as antioxidant, antitumor, hepatoprotective, nephroprotective, antibacterial, antidiabetic, anti-inflammation, brain-protective, and antihyperlipidemic [48,49].

Table 1. HPLC chromatographic analysis of compounds identified in extracts of *S. elaeagnifolium* flowers, fruits, and leaves.

Peak	Standards	Formula	Rt (min)	% Area		
				SEFr	SEFl	SEFe
1	Salicylic acid	$C_7H_6O_3$	7.88	68.39	nd	2.46
2	Ferulic acid	$C_{10}H_{10}O_4$	9.60	2.29	2.57	nd
3	Sinapic acid	$C_{11}H_{12}O_5$	11.30	3.81	1.94	8.35
4	Cinnamic acid	$C_9H_2O_2$	12.40	14.73	nd	nd
5	Chlorogenic acid	$C_{16}H_{18}O_9$	12.55	14.73	9.42	6.70
6	Naringin	$C_{15}H_{12}O_5$	12.95	nd	nd	2.85
7	Quercetin	$C_{10}H_{10}O_4$	13.50	nd	33.32	6.52
8	Rutin	$C_{27}H_{30}O_{16}$	14.53	4.52	5.19	nd
9	Quercetin-3-O-beta-glucoside	$C_{21}H_{20}O_{12}$	15.14	nd	36.99	13.33
10	Kaempferol	$C_{15}H_{10}O_6$	15.70	nd	9.51	36.19
11	Chalcone	$C_{15}H_{12}O$	17.39	nd	nd	4.13

SEFr—extract of fruits; SEFl—extract of flowers; SEFe—extract of leaves.

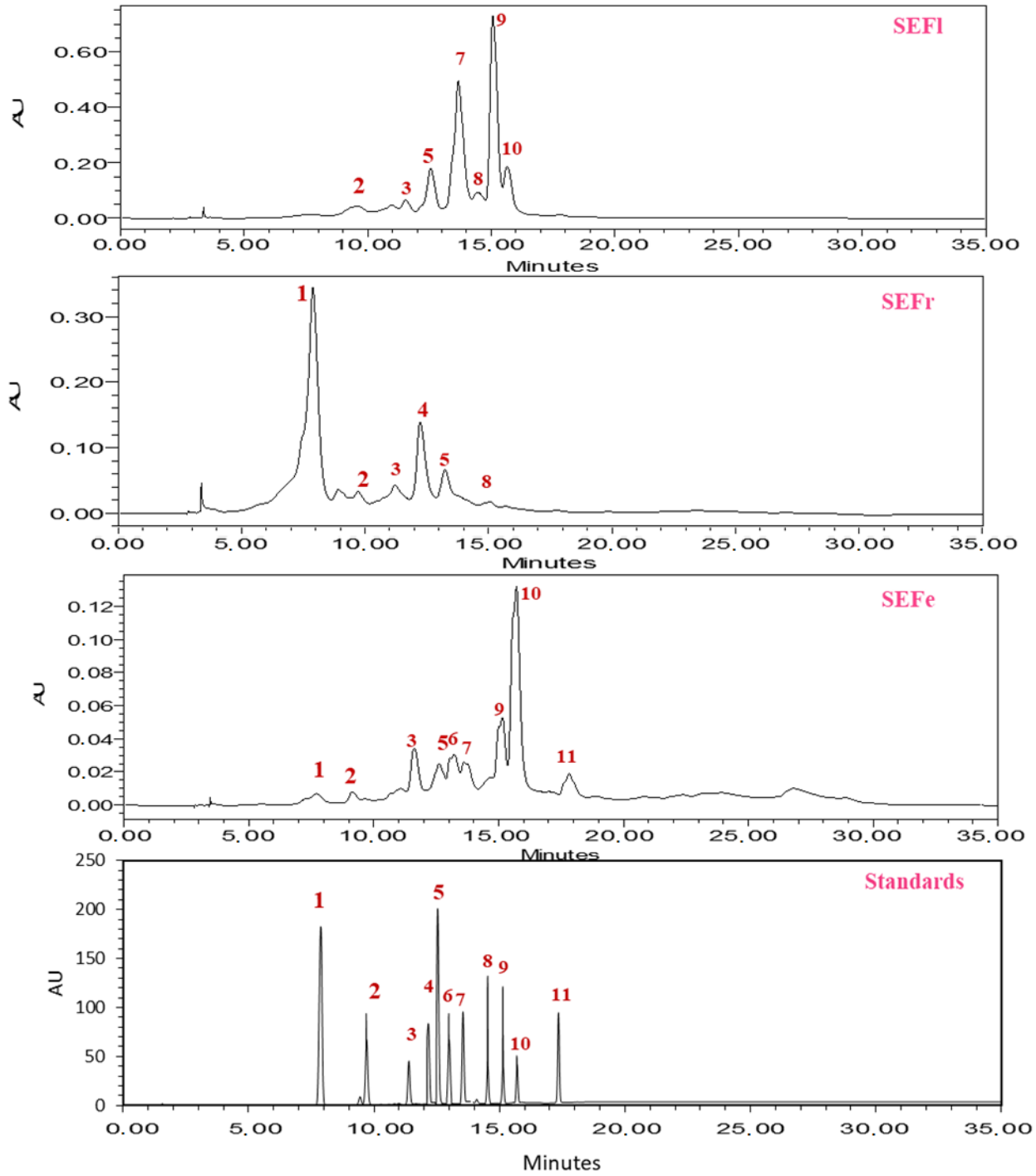
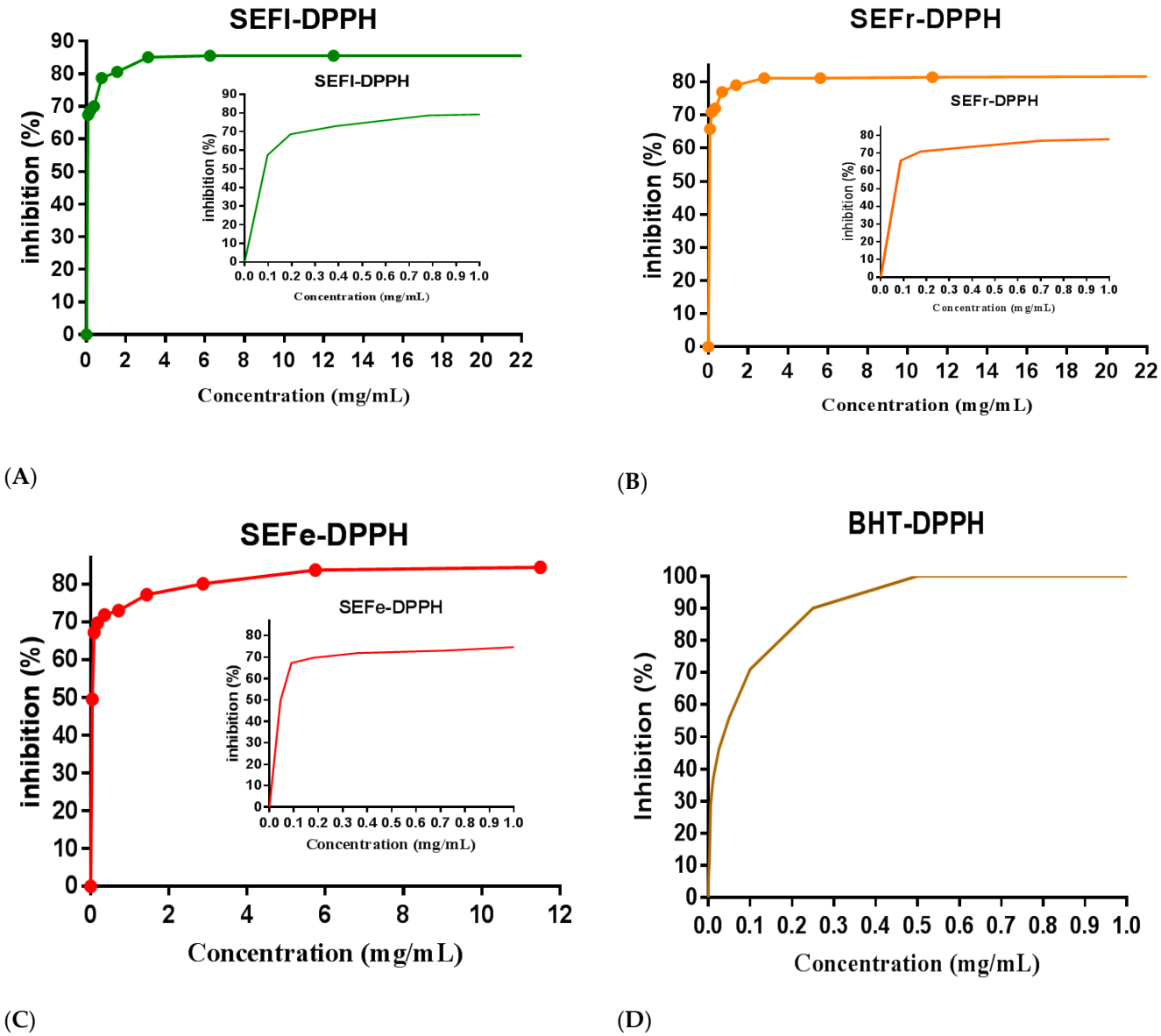


Figure 2. HPLC-DAD chromatogram of *S. elaeagnifolium* extracts—fruits (SEFr), leaves (SEFe), and flowers (SEFl)—at 320 nm using the following standards: salicylic acid (1), ferulic acid (2), sinapic acid (3), cinnamic acid (4), chlorogenic acid (5), naringin (6), quercetin (7), rutin (8), quercetin-3-O-beta-glucoside (9), kaempferol (10), and chalcone (11).

3.2. Antioxidant Activity

Findings showed that the aerial parts of *S. elaeagnifolium* extracts (SFEr, SEFe, and SEFl) possess very important antioxidant properties (Figure 3 and Table 2). Importantly, the IC_{50} for flower, leaf, and fruit extracts were 132.13 ± 5.59 µg/mL, 43.19 ± 1.46 µg/mL, and 71.21 ± 3.87 µg/mL, respectively. The anti-free radical capacity of leaf extract (IC_{50} = 43.19 ± 1.46 µg/mL) was more potent than the standard (BHT,

IC_{50} = 67.17 ± 2.04 µg/mL), and other extracts. This activity may be explained by the existence of polyphenols, such as sinapic acid, cinnamic acid, and chlorogenic acid, as well as flavonoids, such as rutin, and quercetin-3-O-beta-glucoside [50,51].



(**A**) (**B**)

(**C**) (**D**)

Figure 3. Antioxidant capacity of aerial parts of *S. elaeagnifolium*: concentration—% inhibition flowers (**A**), fruits (**B**), leaves (**C**), and BHT (**D**).

Table 2. The IC_{50} and total antioxidant capacity of various extracts of *S. elaeagnifolium* and BHT.

Samples	DPPH-IC_{50} (µg/mL)	TAC (µg AAE/mg)
SEFr	71.21 ± 3.87	900.06 ± 4.01
SEFe	43.19 ± 1.46	792.10 ± 6.72
SEFl	132.13 ± 5.59	681.10 ± 3.02
BHT	67.17 ± 2.04	800.07 ± 3.11

SEFr—extract of fruits; SEFl—extract of flowers; SEFe—extract of leaves.

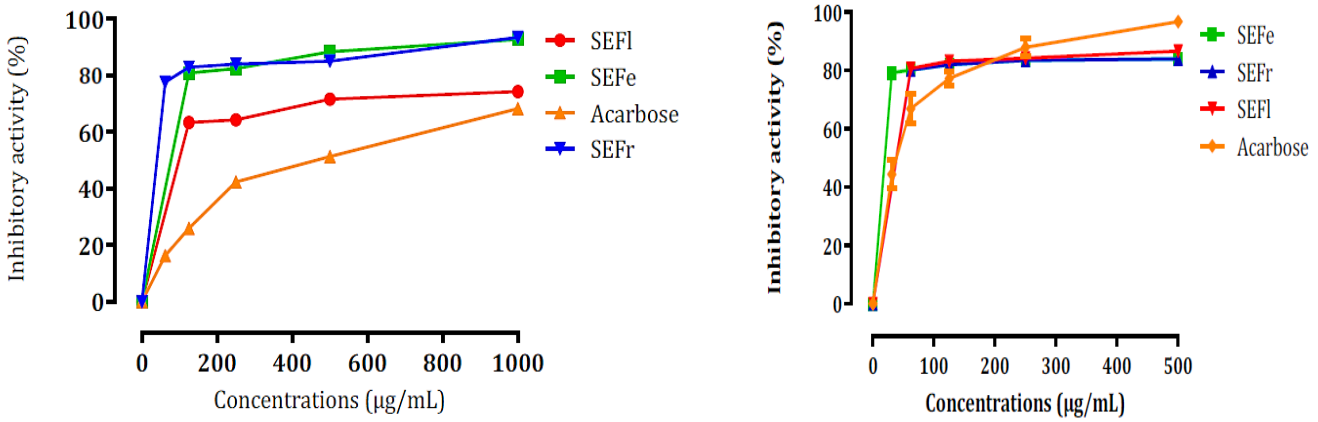
Multiple studies have revealed that the genus *Solanum* possesses antioxidant capacities [26,28,52], which is in agreement with this study. Importantly, the total antioxi-

dant capacity of SEFr, SEFe, and SEFl were determined to be 900.06 ± 4.01 µg AAE/mg, 792.10 ± 6.72 µg AAE/mg, and 681.10 ± 3.02 µg AAE/mg, respectively.

Antioxidants play an important role in preventing pathogenic processes associated with respiratory disorders, cancer, cardiovascular disorders, cataracts, and can also protect the body from oxidation. Natural antioxidants include phenolics, flavonoids, and tannins, among others [53]. Phenolics are prevalently used antioxidant substances in both traditional and modern medicine. Polyphenols act as reducing agents and hydrogen donors by scavenging free radicals; they also act as chelating ions due to their higher redox properties [54]. The ability of flavonoids to hydrogenate promotes hydroxylation of their phenolic rings. This structural feature can be seen in flavonoids, such as kaempferol, quercetin, and myricetin, where the antioxidant activity increases with the number of OH groups in the molecule [55].

3.3. In Vitro Antidiabetic Activity

The results demonstrated that all fractions of *S. elaeagnifolium* (SEFr, SEFl, and SEFe) had very strong anti-α-amylase effects (Figure 4A and Table 3). Notably, SEFe and SEFl were found to possess lower inhibitory activity (IC_{50} = 79.16 ± 40.31 µg/mL, and IC_{50} = 99.16 ± 1.17 µg/mL, respectively) than the positive control, acarbose (IC_{50} = 44.6 ± 0.01 µg/mL). Meanwhile, SEFr was found to possess higher inhibitory activity (IC_{50} = 40.31 ± 2.04 µg/mL) than the positive control and other parts of the plant.



(**A**) (**B**)

Figure 4. The effect of SEFr, SEFl, and SEFe from *S. elaeagnifolium* in vitro in comparison to the control on α-amylase enzyme inhibition (**A**) and α-glucosidase enzyme inhibition (**B**).

Table 3. Inhibition of pancreatic α-amylase and intestinal α-glycosidase by *S. elaeagnifolium* extracts and acarbose.

Samples	IC_{50} (µg/mL)	
	α-Amylase	α-Glycosidase
Acarbose	44.65 ± 0.01	52.56 ± 2.67
SEFl	99.16 ± 1.17	41.14 ± 1.55
SEFe	79.16 ± 2.35	20.05 ± 0.12
SEFr	40.31 ± 2.04	20.53 ± 0.37

SEFr—extract of fruits; SEFl—extract of flowers; SEFe—extract of leaves.

Importantly, *S. elaeagnifolium* extracts (SEFr, SEFe, and SEFl) were found to possess significant anti-α-glucosidase activity (Figure 4B and Table 3), while SEFe (20.05 ± 0.12 µg/mL) inhibited α-glucosidase enzyme more than SEFr (20.53 ± 0.37 µg/mL), followed by SEFl (41.14 ± 1.55 µg/mL). Notably, all three extracts possessed higher α-glucosidase activity

than the positive control (52.56 ± 2.67 µg/mL). *S. elaeagnifolium* leaves showed higher α-glucosidase inhibitory activity than the fruits or flowers; this inhibition was due to the difference in chemical composition of the different parts of the plant, and the number of molecules identified in each sample (Table 1). This activity may have been due to the synergistic effect of the different chemical components of the plant. The solvent used for extraction may also have had an effect on anti-α-glucosidase activity [11,56,57].

Due to an increase in the number of diabetic patients worldwide, there is currently a high demand for antidiabetic agents with no adverse effects on human health, necessitating research into antidiabetic agents derived from medicinal plants [7]. A diverse variety of plants, including those in the genus *Solanum*, have been studied for their antidiabetic properties [5,58,59]

Selvi and Yoganath [60] investigated the antidiabetic activity of stems and leaves from *S. nigrum*, and discovered that the percentage of α-amylase inhibition increased in tandem with increasing concentrations. Plant extracts are largely used to manage diabetes; in particular, *S. trilobatum* was treated with water after formulation and revealed antidiabetic activity [58]. In this sense, *S. virginianum* aqueous and ethanolic extracts inhibited α-amylase, as recorded in the literature [58]. Furthermore, the extract of *S. surattense* leaves exhibited antidiabetic properties [61,62]. In this study, the antidiabetic activity may have been due to the abundance of bioactive components identified by HPLC in the plant extracts that were studied.

In this research study, antidiabetic activity may be attributed to the plant's high concentration of chemical compounds which include naringin, rutin, and quercetin-3-O-beta-glucoside [63]. Of these compounds, naringin possessed the most potent antidiabetic activity via the inhibitory activity of digestive enzymes. The antidiabetic effect of naringin in type 2 diabetic rats was investigated. Naringin supplementation was shown to improve elevated levels of glucose and glycosylated hemoglobin, as well as lower serum insulin levels and hepatic and muscle carbohydrate contents via insulin-resistant hypoglycemic effects [64,65]. This molecule was shown to lower blood glucose and regenerate body weight while trying to normalize serum lipid content and oxidative stress biomarkers in the pancreas and liver, indicating its potential for future drug development as an antidiabetic compound [66]. Comparatively, rutin has been shown to reduce carbohydrate absorption from the small intestine, improve tissue glucose metabolism, suppress tissue glucogenesis, activate insulin secretion by cells, and protect islets from degenerative changes [67]. Many experimental studies have been conducted to assess the hypolipidemic and antihyperglycemic impacts of rutin [68]. Quercetin is a major natural flavonoid, abundant in medicinal plants and fruits—several health benefits, including an antidiabetic effect, have been demonstrated. Quercetin has displayed antidiabetic effects via several mechanisms, including insulin secretion activation, insulin resistance reduction, neurohumoral maintenance, inflammation reduction, and oxidative stress [69].

3.4. In Silico Studies

In antidiabetic activity, the inhibition of DPP-IV represents a major key in the treatment of type 2 diabetes. To investigate the antidiabetic activity of phenolic compounds in *S. elaeagnifolium*, molecular docking was performed in the active site of DPP-IV. The results showed strong inhibitory effects with a range of glide scores from −2.63 to −8.10 Kcal/mol. Rutin was the most potent compound with a glide gscore of −8.10 kcal/mol, a glide emodel of −103.65 kcal/mol, and a glide energy of −74.52 kcal/mol. Quercetin-3-O-beta-glucoside also exhibited significant activity with a glide gscore, glide emodel, and glide energy of −6.23, −68.42, and −52.83 Kcal/mol, respectively. Another compound, chalcone, displayed remarkable activity with a glide gscore, glide emodel, and glide energy of −5.73, −36.06, and −28.21 Kcal/mol, respectively (Table 4).

Table 4. Docking results with phenolic compounds in DPP-IV.

	2RIP		
	Glide Gscore(Kcal/mol)	**Glide Emodel(Kcal/mol)**	**Glide Energy(Kcal/mol)**
Rutin	−8.10	−103.65	−74.52
Quercetin-3-O-beta-glucoside	−6.23	−68.42	−52.83
Chalcone	−5.73	−36.06	−28.21
Naringin	−5.37	−68.48	−53.20
Chlorogenic acid	−5.12	−55.94	−42.80
Kaempferol	−5.07	−47.51	−34.63
Salicylic acid	−4.22	−23.90	−17.91
Sinapic acid	−2.99	−27.59	−22.42
Ferulic acid	−2.96	−26.30	−21.03
Cinnamic acid	−2.63	−17.22	−14.20

In preclinical studies, rutin and quercetin-3-O-beta-glucoside (Q3G) have been investigated for their potential effects on diabetes. Studies suggest that rutin and Q3G may exhibit antidiabetic properties by improving insulin sensitivity, reducing blood glucose levels, and decreasing oxidative stress in animal models [70,71]. Furthermore, chalcones—a class of natural compounds found in plants—have been shown to possess a wide range of pharmacological properties, including antidiabetic effects. Several studies have investigated the potential antidiabetic effects of chalcone, both in vitro and in vivo, and the results are promising [72,73]. According to the research of this in silico study, naringin demonstrated a noteworthy antidiabetic effect. Moreover, several other studies have explored the antidiabetic potential of naringin, revealing that it may improve glucose metabolism, activate the AMPK signaling pathway, and reduce oxidative stress and inflammation through various mechanisms [74,75]. On the other hand, an in vitro study showed that naringin has no effect on alpha-glucosidase [76].

The docking of rutin in the active site of DPP-IV showed the formation of 10 hydrogen bonds with the ARG 125, ASN 710, ARG 669, GLU 206, SER 209, GLN 553, and TYR 547 residues, as well as two Pi-Pi stacking bonds with the TYR 547 residue. Furthermore, quercetin-3-O-beta-glucoside established seven hydrogen bonds in the active site of DPP-IV with the TYR 662, ASN 710, GLU 206, and ARG 669 residues (Figures 5 and 6). Chalcone established a single hydrogen bond with the ASN 710 residue, and two Pi-Pi stacking bonds with the TYR 662 and TYR 666 residues. Moreover, naringin established two hydrogen bonds with residue GLU 206, two Pi-Pi stacking bonds with residues TYR 547 and TRP 629, and a single Pi-cation bond with residue ARG 125 in the active site of DPP-IV (Figures 5 and 6).

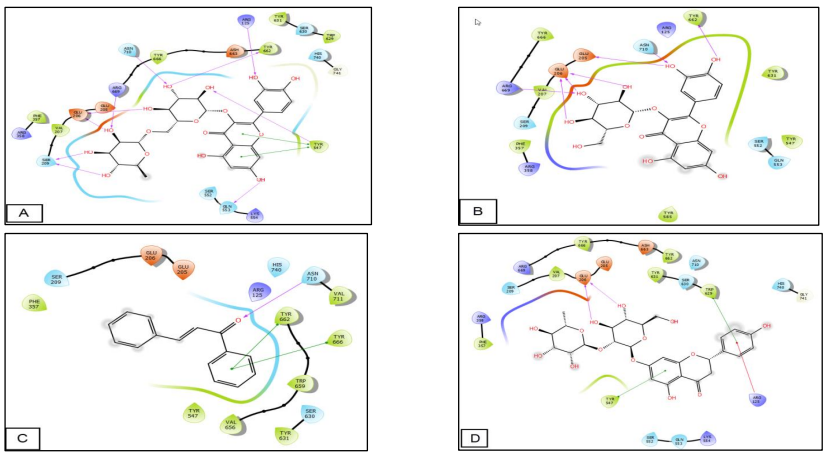


Figure 5. Two-dimensional view of ligand interactions in the DPP-IV active site: (**A**) rutin; (**B**) quercetin-3-O-beta-glucoside; (**C**) chalcone; (**D**) naringin.

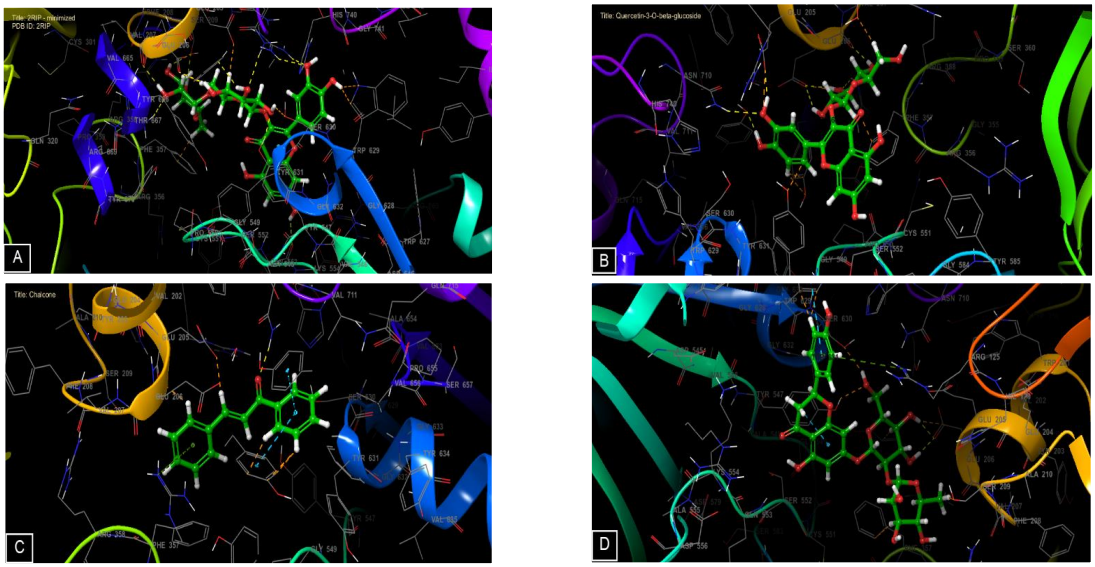


Figure 6. Three-dimensional view of ligand interactions in the DPP-IV active site: (**A**) rutin; (**B**) quercetin-3-O-beta-glucoside; (**C**) chalcone; (**D**) naringin.

4. Conclusions

This study highlighted the chemical composition and the antioxidant and antidiabetic properties of aerial parts of *S. elaeagnifolium*. This plant is found to be rich in polyphenol and flavonoid content, which may determine its diabetic and antioxidant properties, as reported in this work. Further research on toxicity in non-humans is warranted before the use of *S. elaeagnifolium* extracts for medicinal purposes.

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