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Folliculi sennae Extract: A Multifunctional Approach to Alzheimer's and Diabetes

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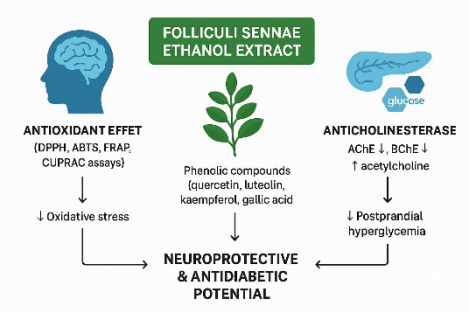
Abstract: Alzheimer's disease (AD) and type 2 diabetes mellitus (T2DM) exhibit overlapping molecular pathways characterized by oxidative imbalance and enzyme dysfunction. This study provides a comprehensive evaluation of the multifunctional potential of *Folliculi sennae* (*F. sennae)* ethanol extract as a natural therapeutic agent targeting these disorders. Phenolic profiling using LC–MS/MS revealed abundant bioactive compounds, including quercetin, luteolin, kaempferol, and gallic acid, with high linearity and reproducibility. The extract exhibited moderate antioxidant activity across DPPH, ABTS, FRAP, and CUPRAC assays, highlighting its redox-modulating capacity. Importantly, enzyme inhibition assays demonstrated notable inhibition of acetylcholinesterase (AChE, IC_{50} = 10.34 µg/mL), butyrylcholinesterase (BChE, IC_{50} = 7.72 µg/mL), and α-glucosidase (IC_{50} = 6.66 µg/mL), indicating potential neuroprotective and antidiabetic effects. These findings suggest that *F. sennae* orchestrates a synergistic interplay between antioxidant defense and targeted enzymatic inhibition, positioning it as a promising multitarget natural candidate for managing oxidative stress–linked neurodegenerative and metabolic disorders. The study lays the biochemical groundwork for future translational research exploring *F. sennae* as a safe, plant-based therapeutic intervention.



Keywords: *Folliculi sennae*, Alzheimer's disease, type 2 diabetes mellitus, antioxidant activity, cholinesterase inhibition.

1 Introduction

Oxidative stress—defined as an imbalance between excessive reactive oxygen species (ROS) production and insufficient antioxidant defense—plays a central role in the development and progression of numerous chronic disorders, including Alzheimer's disease (AD), type 2 diabetes mellitus (T2DM), cardiovascular dysfunction, and age-related degenerative conditions[1-3]. Under normal physiological conditions, antioxidant enzymes such as catalase, superoxide dismutase, and glutathione peroxidase maintain cellular redox homeostasis and safeguard biomolecules against oxidative injury. However, persistent ROS accumulation leads to oxidative modification of proteins, lipids, and nucleic acids, triggering mitochondrial impairment as well as apoptotic and inflammatory cascades[4, 5]. These oxidative and inflammatory pathways represent common molecular intersections that link metabolic dysregulation to neurodegenerative diseases.

AD, the most prevalent, is characterized by progressive neuronal loss, extracellular ß-amyloid (Aß) plaques, tau hyperphosphorylation, and synaptic dysfunction[6, 7]. Increasing evidence indicates that disturbances in redox balance

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and insulin signaling within the brain exacerbate cholinergic neuronal injury and cognitive impairment[8]. Acetylcholine (ACh), is hydrolyzed in the synaptic cleft by acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). Overactivation of these enzymes diminishes ACh availability and accelerates neuronal degeneration[9, 10]. Consequently, cholinesterase inhibition remains a cornerstone in AD therapy. Current drugs such as donepezil, rivastigmine, galantamine, and tacrine provide symptomatic improvement; however, their long-term effectiveness is limited, and adverse reactions—including gastrointestinal disturbances and hepatotoxicity—often restrict their clinical use[11, 12]. Therefore, naturally derived molecules that can simultaneously reduce oxidative stress and inhibit cholinesterases are being extensively explored as safer, multitarget neuroprotective candidates.

T2DM is another multifactorial disorder strongly influenced by oxidative stress and impaired insulin signaling.. Postprandial hyperglycemia mainly results from rapid enzymatic hydrolysis of dietary polysaccharides by α-amylase and α-glucosidase in the intestinal mucosa[13, 14]. Inhibition of these enzymes effectively delays glucose absorption and mitigates postprandial glucose excursions, making it a well-established therapeutic approach. While synthetic inhibitors such as acarbose and voglibose are clinically useful, their long-term administration frequently induces gastrointestinal discomfort[15, 16]. Consequently, natural polyphenolic compounds with α-glucosidase and α-amylase inhibitory activity have gained attention as promising alternatives with improved tolerability[17]. Flavonoids and other plant-derived phenolics exhibit well-documented antioxidant and enzyme inhibitory activities, suggesting their utility as dual modulators of oxidative and metabolic pathways[18, 19].

Medicinal plants are an abundant source of bioactive metabolites exhibiting antioxidant, anti-inflammatory, and antidiabetic effects[20, 21]. The *Senna* genus (family Fabaceae) includes species with well-documented pharmacological actions, such as hepatoprotective, antidiabetic, and antioxidant properties[22]. Among these, *Cassia angustifolia* (syn. *Senna alexandrina*) has attracted attention due to its rich content of anthraquinones and polyphenolic compounds demonstrating notable free-radical-scavenging and enzyme-inhibitory potential[23]. However, the biochemical mechanisms underlying the multitarget pharmacological activities of *Folliculi sennae (F. sennae)* have not yet been comprehensively clarified.

The present work aimed to characterize, in detail, the phenolic composition, antioxidant capacity, and enzyme inhibitory potential of *F. sennae* ethanol extract, emphasizing its multitarget relevance for AD and T2DM management. The phenolic composition was quantified through a highly sensitive liquid chromatography–tandem mass spectrometry (LC–MS/MS) technique. Antioxidant capacity was subsequently analyzed using DPPH (2,2-diphenyl-1-picrylhydrazyl), Ferric Reducing Power Assay (FRAP), ABTS (2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)), and Cupric Reducing Antioxidant Capacity (CUPRAC) methods. Furthermore, inhibitory effects on AChE, BChE, and α-glucosidase were systematically evaluated. To our knowledge, this study represents the first integrated evaluation of the redox-modulating, neuroprotective, and antidiabetic mechanisms of *F. sennae*, highlighting its potential as a safe and multifunctional natural source for future drug development targeting oxidative and metabolic disorders.

2 Material and Methods

2.1 Chemicals

All chemicals and reagents employed in the present study were of analytical grade (purity ≥ 99%). Enzymes, including acetylcholinesterase (AChE, EC 3.1.1.7, Type VI-S, *Electrophorus electricus*), butyrylcholinesterase (BChE, EC 3.1.1.8, equine serum), and α-glucosidase (EC 3.2.1.20, *Saccharomyces cerevisiae*), were supplied by Sigma–Aldrich (St. Louis, MO, USA). Substrates such as acetylthiocholine iodide (ATCI), butyrylthiocholine iodide (BTCI), and *p*-nitrophenyl-α-D-glucopyranoside (*p*-NPG), along with the chromogenic reagent 5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB), were obtained from the same source. Reference antioxidant compounds—Trolox, butylated hydroxytoluene (BHT), and butylated hydroxyanisole (BHA)—served as positive controls. Solvents including ethanol, methanol, and dimethyl sulfoxide (DMSO) were of HPLC grade and used directly without additional purification. Ultrapure water was generated through a Milli-Q system (Millipore, Bedford, MA, USA).

2.2 Preparation of the extract

F. sennae was collected in Gaziantep province during the ripening period between May and June 2022. Fresh leaves of *F. sennae* were collected from naturally growing plants, authenticated by a botanist, and air-dried under shade in a well-ventilated environment to prevent photochemical degradation of phenolics. The dried material was ground into fine powder and extracted using ethanol, a solvent known for its efficiency in isolating both polar and moderately non-polar bioactive compounds. Briefly, 10 g of powdered sample was mixed with 100 mL of ethanol (1:10, w/v) and agitated at room temperature (25 ± 2 °C) for 16 h using a rotary shaker. The mixture was filtered through Whatman No. 1 paper,

and the solvent was evaporated under reduced pressure at 40 °C with a rotary evaporator (Heidolph, Germany). The concentrated extract was weighed, transferred into amber glass vials, and stored at 4 °C until analysis. This extraction procedure was adapted from Işık et al. and modified according to Altın et al.[24, 25].

2.3 LC–MS/MS analysis of phenolic profile

The phenolic composition of the *F. sennae* ethanol extract was determined using a validated LC–MS/MS protocol to achieve accurate identification and quantification[26, 27]. Chromatographic separation was carried out on an Inertsil ODS-4 C18 column (3.0 × 100 mm, 2 µm) maintained at 40 °C. The mobile phase comprised solvent A (water containing 0.1% formic acid) and solvent B (methanol containing 0.1% formic acid), applied at a flow rate of 0.5 mL min^{-1} using a linear gradient. Sample injections were set at 4 µL. Detection and quantification employed multiple reaction monitoring mode. Calibration curves were prepared for each reference standard, with R^2 values exceeding 0.99.All experiments were performed in triplicate, and results are expressed as mean ± SD.

2.4 Enzyme inhibition assays

2.4.1 Cholinesterase (AChE and BChE) inhibition

Cholinesterase inhibition was evaluated following the Ellman spectrophotometric method[28]. The reaction mixture (total volume = 250 µL) contained 50 µL of DTNB (10 mM), 100 µL of Tris–HCl buffer (1 M, pH 8.0), 50 µL of enzyme solution (0.385 U for AChE and 0.880 U for BChE), and 50 µL of extract solution at varying concentrations. After preincubation at 30 °C for 15 min, the reaction was initiated by adding the corresponding substrate (ATCI or BTCI). The absorbance was recorded at 412 nm using a UV-Vis spectrophotometer. The percentage inhibition was calculated relative to control activity, and IC_{50} values were determined from non-linear regression of inhibition curves. All experiments were performed in triplicate to ensure precision and reproducibility.

2.4.2 α-Glucosidase inhibition

The inhibitory effect of the extract on α-glucosidase was evaluated following the protocol of Tao et al.[29] with minor modifications. The assay mixture (200 µL) consisted of 50 µL enzyme solution (0.5 U/mL in phosphate buffer, pH 6.8), 50 µL of the extract, and 50 µL of *p*-nitrophenyl-D-glucopyranoside (*p*-NPG) as the chromogenic substrate.. After incubation at 37 °C for 30 min, the reaction was stopped by adding 50 µL of 0.1 M sodium carbonate (Na_2CO_3). Absorbance was measured at 405 nm using a UV-Vis spectrophotometer and enzyme inhibition was calculated relative to blank controls. Acarbose was used as the reference inhibitor, and IC_{50} values were derived from concentration–response curves. All experiments were performed in triplicate to ensure precision and reproducibility.

2.5 Antioxidant activity assays

2.5.1 Free radical scavenging (DPPH and ABTS)

The DPPH and ABTS radical scavenging activities were assessed using established spectrophotometric protocols[25, 30-32]. For DPPH, 1 mL of extract samples (10–40 µg/mL) was mixed with 0.1 mM DPPH in methanol and incubated for 30 min in the dark. Absorbance was read at 517 nm using a UV-Vis spectrophotometer. For ABTS, the $ABTS^{\bullet+}$ radical cation was produced by reacting 2 mM ABTS with 2.45 mM potassium persulfate, incubated for 14 h in the dark, and diluted to an absorbance of 0.70 ± 0.02 at 734 nm. The extract was added, and absorbance reduction was measured after immediately after addition of the extract. Results were expressed as % radical scavenging inhibition to quantify antioxidant potential, and the methodology is supported by previous studies for correlating phenolic content with radical scavenging activity.

2.5.2 Ferric reducing antioxidant power (FRAP)

The ferric reducing power of the extract was determined using a modified FRAP protocol[33, 34]. Aliquots of the extract (10–40 µg/mL) were combined with 1% potassium ferricyanide and 0.2 M phosphate buffer (adjusted to pH 6.6 to maintain optimal reaction conditions), then incubated at 50 °C for 20 min. Following the addition of 10% trichloroacetic acid (TCA) and centrifugation, the resulting supernatant was mixed with 0.1% ferric chloride ($FeCl_3$), and absorbance was recorded at 700 nm using a UV-Vis spectrophotometer with higher absorbance values indicating increased ferric ion reducing capacity. All measurements were performed in triplicate, and the results were interpreted as quantitative indicators of the extract's electron-donating and overall antioxidant potential[35].

2.5.3 Cupric ion reducing antioxidant capacity (CUPRAC)

The CUPRAC assay was carried out according to the approach of Apak et al. [36, 37] with minor adaptations. Reaction mixtures were prepared by combining 1 mL of 0.01 M $CuCl_2$, 1 mL of ammonium acetate buffer (pH 7.0 to ensure optimal reaction conditions), 1 mL of 2,9-dimethyl-1,10-phenanthroline (neocuproine, 7.5 mM) and 1 mL of the extract solution, followed by incubation at room temperature for 30 min. Absorbance was measured at 450 nm using a UV-Vis

spectrophotometer, with higher values indicating enhanced cupric ion reducing capacity. All experiments were performed in triplicate to ensure reproducibility, and the methodology is supported for correlation of phenolic content with antioxidant activity[38].

2.6 Statistical analysis

To ensure reliability and reproducibility, all assays were carried out in triplicate under uniform experimental conditions. Data are presented as mean ± standard deviation (SD) to reflect variation among replicates. Statistical evaluations were performed using GraphPad Prism (version 8.0; GraphPad Software, San Diego, CA, USA), a tool commonly utilized for detailed biostatistical analysis and graphical representation in biomedical research. Group comparisons were conducted using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test when appropriate. A p value below 0.05 ($p < 0.05$) was considered statistically significant.

3. Results and Discussion

3.1 Phenolic composition of the *F. sennae* extract

The LC–MS/MS analysis revealed a diverse and quantifiable phenolic composition in the ethanol extract of *F. sennae* (**Table 1**). A total of 20 phenolic compounds were identified with high analytical accuracy ($R^2 > 0.99$). Among the detected metabolites, kaempferol (2999.88 μg L^{-1}) and luteolin (2426.45 μg L^{-1}) were the predominant flavonoids, while fumaric acid (1159.88 μg L^{-1}) and vanillic acid (965.79 μg L^{-1}) represented the major phenolic acids. Quantified levels included quercetin (1312.35 μg L^{-1}), phloridzin dihydrate (631.35 μg L^{-1}), and resveratrol (168.96 μg L^{-1}) were also quantified, whereas minor contributions from caffeic acid (88.67 μg L^{-1}), ellagic acid (132.69 μg L^{-1}), and gallic acid (10.18 μg L^{-1}) were detected.

The predominance of kaempferol and luteolin agrees with previous phytochemical investigations on *Senna* species, where these flavonoids were identified as chemotaxonomic markers[22, 23]. Structurally, both compounds possess catechol and hydroxyl moieties on the B-ring, enhancing their electron-donating ability and conferring notable radical-scavenging and metal-chelating properties[21]. These features contribute to phenoxyl radical stabilization and high antioxidant efficiency.

The presence of fumaric and vanillic acids further supports previous reports linking *Senna*-derived phenolic acids to hepatoprotective and anti-inflammatory activities through modulation of NF-κB signaling and oxidative stress pathways[18, 19]. Overall, the data indicate that *F. sennae* is a rich natural reservoir of pharmacologically active phenolics, potentially relevant for managing oxidative stress–associated disorders.

Table 1 The Phenolic content of *F. sennae* ethanol extract.

Standard compounds	[a]LOD/LOQ (μg/L)	Recovery (%)	[b]RT	Concentration (μg/L)
Quercetin	22.5/25.7	1.001	3.879	1312.35
Acetohydroxamic Acid	2.8/8.2	1.000	0.354	198.66
Catechin hydrate	8.2/11.4	0.994	2.692	2.07
Vanillic Acid	125.5/142.2	1.001	3.520	965.79
Resveratrol	9.0/13.6	0.998	3.192	168.96
Fumaric Acid	25.2/31.3	0.997	0.506	1159.88
Gallic Acid	0.90/1.6	1.000	1.429	10.18
Caffeic Acid	6.3/10.7	1.009	2.750	88.67
Phloridzin dihydrate	61.0/207.0	1.000	3.208	631.35
Oleuropein	0.05/1.0	0.997	4.569	33.50
Ellagic Acid	0.101/0.333	1.002	3.875	132.69
Myricetin	55.4/59.6	0.999	3.568	14.45
Protocatechuic Acid	30.3/35.4	1.011	–	*ND*
Butein	22.7/28.6	0.996	3.856	48.49
Naringenin	5.4/6.4	0.998	–	*ND*
Luteolin	0.5/2.5	1.007	3.978	2426.45
Kaempferol	206.6/214.3	0.999	4.109	2999.88
Alizarin	65.2/77.5	0.966	–	*ND*
4-Hydroxybenzoic Acid	30.5/40.25	0.996	3.528	11.23

a LOD/LOQ: limit of detection/limit of quantitation.

b RT: retention time. ND: not detected.

3.2 Antioxidant activities

The antioxidant potential of the *F. sennae* ethanol extract was evaluated using four complementary assays: DPPH, ABTS, FRAP, and CUPRAC (**Table 2**). The extract exhibited measurable free radical scavenging ability, with of 1.864 ± 0.135 % in the DPPH assay and 5.682 ± 0.735 % in the ABTS assay. Although these results were lower than those of the reference antioxidants (BHT and Trolox), the extract demonstrated a distinct antioxidant capacity, confirming the presence of bioactive redox compounds.

In the metal-reducing assays, the extract showed absorbance values of 0.129 ± 0.01 in the FRAP test and 0.191 ± 0.01 in the CUPRAC test, supporting its notable electron-donating and metal ion–reducing potential. These findings indicate that *F. sennae* contains phenolic constituents capable of maintaining redox homeostasis through multiple mechanisms.

The antioxidant activity of *F. sennae* can be primarily attributed to its abundant polyphenolic content—especially kaempferol, luteolin, and resveratrol—which are well-documented for their effective radical-scavenging and metal-chelating effects[1, 21, 24]. Structural studies have revealed that the number and position of hydroxyl groups on the flavonoid B-ring significantly enhance hydrogen-donating capacity and stabilize phenoxyl radicals, thus improving overall antioxidant efficacy[39, 40]. Additionally, fumaric acid contributes to the extract's redox-regulating ability by supporting NADPH-dependent antioxidant enzyme systems and modulating mitochondrial oxidative balance[3, 5].

From a biomedical standpoint, antioxidant-rich botanicals such as *F. sennae* play a crucial role in mitigating oxidative stress–mediated cellular damage. The polyphenolic components of the extract may preserve neuronal integrity by reducing ß-amyloid–associated oxidative burden in AD and improving insulin sensitivity in T2DM [2, 4, 6]. These findings indicate that *F. sennae* could contribute to redox regulation and may offer multitarget effects relevant to neurodegenerative and metabolic disorders, warranting further investigation.

Although the phenolic constituents quantified by LC–MS/MS—such as luteolin, kaempferol, and quercetin—are commonly associated with well-documented antioxidant potential, the extract's DPPH and ABTS scavenging values were comparatively low. Reassessment of the experimental procedures confirmed that these data accurately reflect the extract's behavior in direct radical-quenching assays. This finding is consistent with evidence showing that many flavonoids in plant matrices occur predominantly in glycosylated forms, which possess weaker electron-donating and hydrogen atom–transfer capacity than their aglycone analogues. Recent studies from Guzel and co-workers demonstrated that glycosylated phenolics frequently exhibit reduced DPPH/ABTS activity despite high total phenolic content, highlighting the influence of structural features on assay outcomes[41, 42]. In addition, indirect antioxidant pathways—such as modulation of endogenous redox enzymes or metal chelation—are not fully captured by these assays, which primarily measure single-mode radical scavenging. Therefore, the observed results do not imply low antioxidant efficacy but rather reflect the mechanistic diversity of the extract's phenolic constituents and the methodological specificity of the assays employed.

3.3 Enzyme inhibition activities

3.3.1 Cholinesterase inhibition

The ethanolic extract of *F. sennae* exhibited notable inhibitory activity against both AChE and BChE, with IC_{50} values of 10.34 ± 1.32 µg/mL (R^2 = 0.959) and 7.72 ± 0.92 µg/mL (R^2 = 0.996), respectively (**Table 3**). Although these activities were weaker than those of the standard reference compound tacrine (AChE: 3.19 ± 0.27 µg/mL, R^2 = 0.990; BChE: 2.54 ± 0.09 µg/mL, R^2 = 0.988), the extract still demonstrated significant enzyme inhibition. These findings indicate that *F. sennae* possesses considerable cholinesterase-modulating capacity, suggesting its potential utility as a natural therapeutic candidate for the management of AD.

Table 2 Radical removal and metal reduction activity *F. Sennae*.

Antioxidants	DPPH[a] (0.2 mg mL^{-1})	ABTS[a] (0.2 mg mL^{-1})	FRAP Assay[b] (0.2 mg mL^{-1})	CUPRAC Assay[b] (0.2 mg mL^{-1})
Folliculi sennae	1.864± 0.135	5.682±0.735	0.129±0.01	0.191± 0.01
BHT	49.623± 4.26	45.69±2.582	0.584± 0.04	0.582 ± 0.04
Trolox	76.531± 6.97	80.18± 6.432	0.212± 0.01	0.506± 0.03

Standard antioxidants (BHT, butylated hydroxytoluene, trolox).

[a] Values are expressed as percent radical scavenging activity.

[b] Values are expressed as absorbance. High absorbance indicates high metal reduction capacity.

BHT: butylated hydroxytoluene; Trolox: 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid.

From a neurobiochemical standpoint, impairment of the cholinergic system is a major hallmark of AD, characterized by diminished ACh synthesis and synaptic transmission [43]. Cholinesterase inhibitors delay ACh degradation in synaptic clefts, thereby restoring cognitive and behavioral functions[9, 10]. The concurrent inhibition of AChE and BChE is particularly important because BChE progressively replaces AChE as the disease advances, making dual inhibition a valuable therapeutic approach[11].

The inhibitory profile observed in *F. sennae* may be largely attributed to its high flavonoid content—especially quercetin, luteolin, and kaempferol—which can interact with the catalytic and peripheral anionic sites of cholinesterases via hydrogen bonding and π–π interactions[25, 44]. Such interactions enhance the stabilization of ACh within the synaptic cleft and mitigate oxidative stress–mediated neuronal injury[1,45]. Furthermore, plant-derived dual cholinesterase inhibitors represent safer alternatives to synthetic drugs due to their multifactorial actions, including anti-inflammatory and antioxidant properties[19, 20, 25].

These findings suggest that *F. sennae* may serve as a natural neuroprotective candidate for the management of cholinergic dysfunction in neurodegenerative diseases.

3.3.2. α-Glucosidase inhibition

The *F. sennae* ethanol extract exhibited significant inhibitory activity against α-glucosidase, with an IC_{50} value of 6.66 ± 0.42 μg/mL (R^2 = 0.911), comparable to the standard inhibitor acarbose (IC_{50} = 3.15 ± 0.17 μg/mL, R^2 = 0.996) (**Table 3**; **Fig. 1**). This marked enzyme inhibition indicates that *F. sennae* may represent a promising natural source of α-glucosidase inhibitors for managing postprandial hyperglycemia.

The α-Glucosidase (EC 3.2.1.20) catalyzes the terminal step of carbohydrate digestion by hydrolyzing oligosaccharides into absorbable monosaccharides. Inhibition of this enzyme delays intestinal glucose absorption, effectively reducing postprandial glycemic spikes—a major therapeutic target in T2DM[13-15, 29]. Moreover, α-glucosidase inhibition can attenuate oxidative stress–mediated complications, including mitochondrial dysfunction and neuronal injury, commonly observed in T2DM and AD [46, 47].

Table 3 Inhibitory potential of F. sennae ethanol extract against selected metabolic enzymes.

Inhibitors	AChE IC_{50} (μg/mL)	R^2	BChE IC_{50} (μg/mL)	R^2	α-Glucosidase IC_{50} (μg/mL)	R^2
F. sennae ethanol extract	**10.34 ± 1.32**	**0.931**	**7.72 ± 0.92**	**0.996**	**6.66 ± 0.42**	**0.843**
Tacrine	**3.19 ± 0.27**	**0.979**	**2.54 ± 0.09**	**0.996**	–	–
Acarbose	–	–	–	–	**3.15 ± 0.17**	**0.993**

IC_{50} values represent the mean ± SD of triplicate measurements. Higher R^2 values indicate good model fit reliability.

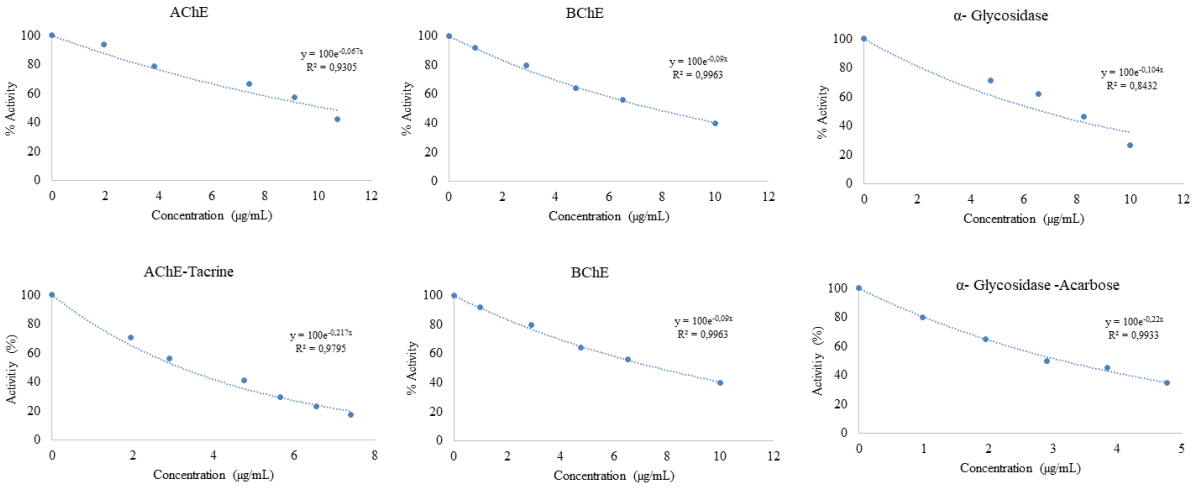

Fig. 1 Inhibition effect of *F. sennae* ethanol extract on AChE, BChE and α-glucosidase.

The inhibitory potential of *F. sennae* is attributed to its high content of phenolic acids (fumaric, caffeic, and vanillic acids) and flavonoids (kaempferol, luteolin, and resveratrol), which can interact with the catalytic and peripheral binding sites of α-glucosidase through hydrogen bonding and hydrophobic interactions[14, 15, 24, 25, 31]. These compounds also modulate glucose metabolism by improving insulin sensitivity and suppressing oxidative stress–induced β-cell apoptosis[3, 4, 6].

From a biomedical perspective, the α-glucosidase inhibition exhibited by *F. sennae* supports its potential role in glycemic regulation[16, 17]. Its antidiabetic, antioxidant, and neuroprotective effects align with evidence that natural phenolics modulate metabolic and neurodegenerative pathways [46, 47]. To the best of our knowledge, this is the first report describing the simultaneous inhibition of AChE, BChE, and α-glucosidase by *F. sennae*, offering new insights into its multifunctional therapeutic potential for oxidative stress–related disorders.

3.4 Clinical and biochemical ımplications

The combination of measurable antioxidant activity and notable enzyme inhibitory properties of *F. sennae* positions it as a promising candidate for the prevention or management of metabolic and neurodegenerative disorders. Oxidative stress is a central mechanism underlying both diabetes and neurodegeneration; therefore, phenolic compounds capable of targeting redox imbalance and enzyme dysfunction possess significant therapeutic potential[48].

Recent studies have demonstrated that, in addition to its antioxidant capacity, *F. sennae* can inhibit α-glucosidase and cholinesterase enzymes. Furthermore, the extract's ability to modulate α-glucosidase and cholinesterase activity suggests a dual role in both glycemic regulation and neuroprotection, which may hold relevance for conditions such as T2DM and AD [49].

However, further studies using in vivo models and molecular interaction analyses are necessary to evaluate its bioavailability, metabolic stability, and overall safety. Such research is essential to validate its clinical applicability and support its use in therapeutic interventions.

4 Conclusion

The ethanol extract of *F. sennae* exhibited considerableinhibitory effects against AChE, BChE, and α-glucosidase, underscoring its dual potential in neuroprotection and glycemic regulation. This study provides the first comprehensive evidence linking the bioactive constituents of *F. sennae* to major enzymatic targets implicated in both neurodegenerative and metabolic disorders. By scientifically validating the plant's traditional therapeutic use, the findings highlight its value as a natural multitarget agent with pharmacological significance. Further in vivo and clinical studies are warranted to elucidate its pharmacokinetics, safety profile, and therapeutic efficacy. Collectively, these results position *F. sennae* as a promising phytotherapeutic candidate for developing novel interventions targeting the interconnected mechanisms of oxidative stress, enzyme dysregulation, and chronic disease progression.

Author Contributions

Turkan Guney: İnvestigation, writing - original draft, writing - review & editing. **Sevgi Altın**: Methodology, investigation, writing - original draft. **Emrah Dikici**: Methodology, validation, writing - original draft. **Mesut Işık**: Methodology, conceptualization, investigation, project administration, writing - original draft, writing - review & editing. **Ekrem Koksal**: Conceptualization, project administration, writing - review & editing.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data will be made available on request.

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