Multi-Target Pharmacological Potential of Selected Medicinal Plant Extracts: Antioxidant, Antimicrobial, and Neuroprotective Activities

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Abstract

The increasing prevalence of neurodegenerative and metabolic illnesses worldwide demands innovative treatment approaches. Medicinal plants having known traditional usage, such as *Terminalia chebula*, *Portulaca oleracea*, and *Artemisia judaica*, are abundant in bioactive chemicals. The purpose of this study is to examine their potential as natural remedies by examining their phytochemical composition and multi-target biological activity. Numerous phytoconstituents, including as phenols, flavonoids, and tannins, have been found to be present by both qualitative and quantitative investigations. *T. chebula* showed the greatest quantities of these compounds. *T. chebula* exhibited the strongest antioxidant activity (DPPH IC_{50} = 13.64 µg/mL), considerable α-amylase inhibition (IC_{50} = 60.11 µg/mL), and moderate pancreatic lipase inhibition (IC_{50} = 468.52 µg/mL) in in vitro bioassays, suggesting strong anti-diabetic and anti-obesity capability. The effects of *A. judaica* and *P. oleracea* were less pronounced. According to antimicrobial examination, *T. chebula* and *A. judaica* shown significant broad-spectrum activity against *Candida albicans*, Gram-positive, and Gram-negative bacteria. Using whole-cell patch-clamp electrophysiological tests, it was shown that all extracts were antagonists of AMPA receptor subunits (GluA1, GluA2, GluA1/2, GluA2/3), with *T. chebula* showing the most potent inhibitory action. According to this study, *Terminalia chebula* is the most effective extract, exhibiting notable multi-target bioactivity against neurological, microbiological, and metabolic targets. The findings support its long-standing application and emphasize its potential as a source of new medicinal compounds. Incorporating these results supports the ongoing investigation of plant extracts in contemporary drug research.

Introduction

The food, cosmetic, pharmaceutical, and fragrance sectors continue to rely heavily on plants as sources of medicinal chemicals. Since obesity affects around 38% of people worldwide and is associated with comorbid conditions including diabetes, heart disease, and cancer, their function is becoming more and more important [1–4]. Natural compounds produced from plants have important metabolic, antioxidant, and antibacterial advantages, including possible ways to combat antibiotic resistance, given the essential role that oxidative stress plays in chronic illnesses [5].

One important component of neurodegeneration is oxidative stress, which both causes and results from disease pathology [6]. Antioxidants from plants have therapeutic promise because they reduce oxidative damage to the neurological system [7]. Because of their function in synaptic control and potential for therapeutic intervention, ionotropic glutamate receptors, especially AMPA receptors, are important molecular targets within the central nervous system [8–10].

Medicinal plants with significant medicinal potential include *Terminalia chebula*, *Portulaca oleracea*, and *Artemisia judaica*. Traditional medicine has traditionally utilized *A. judaica*, often referred to as Judean wormwood, to cure fever, infections, and inflammation [15]. It is indigenous to the Mediterranean, Red Sea, Gabal Elba, and Sinai areas of Egypt. Essential oils, triterpenes, flavonoids, and sesquiterpene-lactones are all detected by phytochemical studies. *A. judaica* extracts show a variety of pharmacological actions, such as hypoglycemic, antioxidant, antimicrobial, antiangiogenic, and renoprotective effects; its essential oil has anti-inflammatory, analgesic, antipyretic, anthelmintic, and repelling qualities [16, 17].

Purslane, or *Portulaca oleracea*, is a plant that is used medicinally across the Mediterranean, Central Europe, and Asia [18, 19]. It exhibits a variety of pharmacological characteristics and is abundant in flavonoids, alkaloids,

polysaccharides, omega-3 fatty acids, and vitamins A, C, E, and B-complex. High quantities of dopamine and noradrenaline found in its leaves promote healthy immune system activity (20). Oleraceins are examples of bioactive substances that support therapeutic and antioxidant properties. Purslane has been linked to anti-inflammatory, antidiabetic, and anticancer properties, highlighting its significance in medicine and nutrition [21, 22].

Terminalia chebula (*T. chebula) is* a species known as the "King of Medicine" in Tibet. The plant has high medicinal value and has been found to have various antidiabetic [23], antioxidant, and anti-inflammatory properties, suggesting potential applications in nutraceuticals, functional foods, and pharmaceutical industries [23]. Similarly, *T. chebula* is a plant rich in phytoconstituents like tannins, flavonoids, sterols, amino acids, fructose, resin, and fixed oils, with about 32% tannin content [25, 26].

This study aims to evaluate the phytochemical profile and pharmacological effect (anti-obesity, antidiabetic, antioxidant, and antimicrobial properties) of different extracts from *Artemisia judaica*, *Portulaca oleracea*, and *Terminalia chebula*. Moreover, the study will examine the effect of extracts on the kinetics of AMPA receptor subunits and neurodegenerative disorders.

Material and methods

Reagents and Chemicals

NaOH, Methanol, n-Hexane, and Acetone were obtained from Loba Chemie (India). Benedict's reagent, Millon's reagent, and Ninhydrin solution were purchased from Alfa Agar (England). Alfa-Aesar (England) supplied the iodine solution, H_2SO_4, and Molisch's reagent. HCl, Folin-Ciocalteu's reagent, Potassium acetate, Chloroform, $AlCl_3$, and DPPH (2,2-Diphenyl-1-picrylhydrazyl) were obtained from Sigma-Aldrich (Germany). Magnesium ribbon, acetic acid, $FeCl_3$, and DMSO (dimethyl sulfoxide) were acquired from Riedel-de Haen (Germany). α-Amylase was obtained from Sigma (Mumbai, India), DNSA (3,5-dinitrosalicylic acid) reagent from Sigma (LA, USA), and Acarbose from Sigma (St. Louis, USA). Trolox ((s)-(-)-6 hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) and quercetin were purchased from Sigma-Aldrich (Denmark). Tris-HCl buffer, Orlistat, and p-nitrophenyl butyrate were also obtained (Denmark).

Plants materials

All investigated medicinal plants in this study were purchased from different herbalists in the West Bank area of Palestine. The taxonomical characterizations of *A. Judaica, P. oleracea* and *T. chebula* plants were conducted by Prof. Dr. Nidal Jaradat in the Herbal Products Laboratory at An-Najah National University and kept under the voucher specimen number of Pharm-PCT-238, Pharm-PCT-1935, and Pharm-PCT-2812, respectively. Each dried plant was ground by a mechanical grinder (Moulinex, model LM2211, UNO, Shanghai, China) into a fine powder, labeled, and transferred into airtight containers for future use in our study and other experiments.

Crude aqueous plant extracts for phytochemical screening and biological activities evaluation

Each medicinal plant was subjected to an exhaustive aqueous extraction by mixing 200 ml of distilled water with 5 g of each powdered plant in a beaker. The mixture was heated to reach 40 ºC on a hot plate while constantly swirling for 20 minutes. The hot mixtures were filtered individually using Whitman filter paper (Machrery-Nagel, Bethlehem, PA, USA; MN 617 and Whatman no. 1). The aqueous extract fraction was dried using a freeze dryer (Mill Rock Technology, model BT85, Danfoss, Shanghai, China). The extraction yields for *A. Judaica, P. oleracea*, and *T. chebula* were 1.9 ± 0.4, 5.6 ± 0.91, and 4.5 ± 0.9% (w/w), respectively, and stored at 2 to 8 ºC until needed [27].

Extraction yield was calculated using the following equation

% Yield = (Weight of *plant* extract /weight of dry plant) × 100%

Phytochemical screening tests for each examined plant extract

Qualitative phytochemical analysis (including proteins, carbohydrates, flavonoids, saponins, glycosides, steroids, and terpenoids) has been carried out for all aqueous extracts [28–31].

Tests for carbohydrates

Fehling's solutions test

a mixture of Fehling solutions A and B was boiled with and equal volumes were added to both crude plants extracts. A red color precipitate indicated the presence of reducing sugars.

Benedict's reagent test

2 ml of Benedict's reagent was boiled with crude extracts; a reddish-brown color indicated the presence of the carbohydrates.

Molisch's solution test

2 ml of Molisch's solution was shaken with crude plants extracts then 2 ml of H_2SO_4 concentrated solution was added and poured carefully along the side of the test tube. A violet ring appeared at the inter phase of the test tube indicated the presence of carbohydrate.

Iodine test

2 ml of iodine solution was mixed with both crude plants extracts. Purple or dark blue colors indicated the presence of starch.

Alkaloids test

The 0.5 g of the plant extract was dissolved in 5 ml of 1% HCl and kept in a water bath for about two minutes. 1 ml of the filtrate was treated with Dragendroff's reagent. Formation of turbidity or precipitation was used as an indicator for the presence of alkaloids.

Tannins and phenols test

About 0.5 g of the sample was dissolved in 10 ml of boiling water and was filtered. A few ml of 6% $FeCl_3$ was added to the filtrate. Formation of deep green color indicates the presence of tannins.

Flavonoids test

About 0.2 g of the extracts were dissolved in methanol and heated for some time. A chip of Mg metal was introduced, followed by adding a few drops of concentrated HCl. The appearance of red or orange was an indicator of the flavonoids.

Saponin test

About 0.5 g of the plant extract was stirred with water in the test tube. Frothing persists on warming was taken as a piece of evidence for the presence of saponin.

Steroids test

The Salkowski technique was utilized for the identification of steroids. A solution containing 0.5 g of extract was dissolved in 3 ml chloroform and then filtered. Concentrated H_2SO_4 was added to the filtrate to create a distinct layer below. A good indication of the presence of a steroid ring was determined based on the observation of a reddish-brown tint.

Test for glycoside

About 0.5 g of the extracts were dissolved in 2 ml of glacial acetic acid containing one drop of 1% $FeCl_3$ and concentrated H_2SO_4. A brown ring obtained at the interphase indicates the presence of deoxy sugar. A violet ring appeared below the ring, while in the acetic acid layer, a greenish ring appeared just above the ring and gradually spread throughout this layer.

Quantitative phenolic content

Spectrophotometric method was used to determine the total phenol content in the three plants' aqueous extracts [32]. Each extract was prepared by dissolving methanolic plant extract, 10% Folin-Ciocalteu's reagent, water, and 7.5% $NaHCO_3$ aqueous solution. The samples were incubated at 45ºC for 45 minutes, and absorbance was measured at 765 nm. The mean absorbance value was determined by triplicating each prepared sample. The same procedure was used for the Gallic acid standard solution, with serial dilutions to create the calibration line.

Quantitative flavonoid content

The total flavonoid content was determined and expressed as mg of quercetin per gram of extract fraction (mg QUE/g fraction) using a previously adapted procedure [33]. Quercetin was dissolved in water to create a 10 mg/ml solution, then diluted to obtain different concentrations (10, 30, 50, 70, and 100 µg/ml). Each solution was mixed with 0.3 ml of sodium nitrite, 0.3 ml of 10% $AlCl_3$, 1 ml of 2 M NaOH, and 1 ml of distilled water. Samples were incubated for 30 minutes at room temperature. Absorbance was measured at 510 nm using a spectrophotometer.

Total tannins content in plant extract fractions

Different concentrations of catechin solution were prepared (10, 30, 50, 70,100µg/ml). Then, 3 mL of 4% vanillin solution, which was added in methanol, and 1.5 mL of concentrated HCl. The mixture was left for 15 min; then absorption was measured at 500 nm against methanol as a blank. Total tannins are expressed as mg (+)-catechin/g plant extract. All samples in this experiment were analyzed in triplicate to ensure informative results. Total tannin in extracts was expressed regarding catechin Equivalents (mg of CA/g of extract fraction).

Assessment of Pancreatic Lipase Inhibition by Aqueous Extracts

Solutions were prepared, including a stock of plant extract in 10% DMSO and five different enzyme concentrations. PNPB (p-nitrophenyl butyrate) was dissolved in acetonitrile to prepare a stock solution. Test tubes containing porcine pancreatic lipase and diluted plant extract solutions were incubated with Tri-HCl buffer at 37°C for 15 minutes. The PNPB solution was added and incubated for 30 minutes at 37°C. Pancreatic lipase activity was determined using a UV-visible spectrometer (Jenway 7135, Staffordshire, UK) by measuring the hydrolysis of p-nitrophenolate to p-nitrophenol at 405 nm. The same procedure was repeated for aqueous and organic extracts, and Orlistat was used as a positive control [34, 35].

α-Amylase Inhibition Assay

The investigation comprised mixing plant extracts with 10% DMSO to make a plant-working solution, diluting it to create different dilutions, and dissolving 12.5 mg of α-amylase enzyme powder in DMSO to create an enzyme stock solution, as previously done [36]. Corn starch solution was also created. The mixture was incubated at 30°C for 10 minutes and then added to the plant extract stock solution. The solution was then replaced with distilled water and cooled. The solution was then boiled in a water bath at 85–90°C for 10 minutes. Acarbose, a commercial anti-amylase medication, was used as a positive control. The optical activity of the prepared solutions was measured at 540 nm using a UV-visible spectrophotometer. Three duplicates of the established tests were run.

Antioxidant activity by free radical scavenging assay

Following previous protocols for antioxidant evaluation [37, 38], a stock solution (1 mg/mL) was made by dissolving 100 mg of plant extract in 100 mL of methanol. Different solution concentrations (2, 3, 5, 7, 10, 20, 30, 40, 50, 80, and 100 µg/mL) were prepared. One milliliter of DPPH was combined with one milliliter of stock solution and one milliliter of methanol. The solution was incubated at room temperature for 30 minutes in the dark. A blank solution was prepared by substituting methanol for the plant extract solution. Trolox (Sigma-Aldrich, St. Louis, MO, USA) was a positive control. Absorbance was measured at 517 nm using a spectrophotometer.

Antimicrobial Assay

The antibacterial and antifungal properties of each aqueous extract were evaluated using six strains from the American Type Culture Collection (ATCC): *Staphylococcus aureus* (ATCC 25923), *Klebsiella pneumoniae* (ATCC 13883), *Proteus vulgaris* (ATCC 8427), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 9027), and *Candida albicans* (ATCC 90028), as well as a clinically confirmed methicillin-resistant *Staphylococcus aureus* (MRSA). The antimicrobial activity of the extracts was determined using the broth microdilution method [39, 40]. Each extract was dissolved and serially micro-diluted (with a concentration gradient from 5 mg/ml to 0.1 mg/ml) 10 times in Mueller-Hinton broth. Micro-wells were inoculated with test microbes and tested in triplicate; the incubation period lasted 18–24 hours for bacterial strains and 48 hours for the *Candida albicans* strain. The

minimum inhibitory concentration (MIC) was determined at the lowest concentration of extract, which showed no visible microbial growth. Known antimicrobial agents such as ampicillin and ciprofloxacin were used for bacterial strains, and fluconazole was used for the fungal strain [41].

Methodological Advances in the Electrophysiological Characterization of AMPA Receptors

In this research endeavor, the construction of AMPA receptor subunits was based on the flip isoform. These constructs, namely GluA1-3 in their Q-form/flip configuration, were initially sourced through the generous provision of S.F. Heinemann from the Salk Institute in La Jolla, California. The chosen cellular model for this study was the HEK293T line, acquired from Sigma, based in Germany. These cells were cultured in an environment consisting of Dulbecco's Modified Eagle Medium (DMEM), procured from Sigma in the United States, supplemented with a 10% inclusion of fetal bovine serum, streptomycin at a concentration of 0.1 mg/ml, and sodium pyruvate at 1 mM, sourced from Biological Industries in Beit-Haemek, Israel. The cells were incubated at a constant temperature of 37°C in an atmosphere containing 5% CO_2. The pRK5 plasmid incorporated wild-type AMPAR DNA into the cellular genome. The plasmid was genetically modified to enable the simultaneous production of an improved form of green fluorescent protein (EGFP), which was acquired from Clontech in Palo Alto, California. This was achieved by a co-transfection procedure that maintained a ratio of 1:9 between pEGFP-C1 and the GluA component. This methodology aimed at optimizing protein expression within the HEK293T cells. The transfection was carried out utilizing jetPRIME, as detailed by Polyplus in New York, NY, consistent with methodologies described in our prior studies (42–44). A 36-hour interval post-transfection was observed before the cells were subjected to either electrophysiological examination or visual analysis using a stereomicroscope (Jenway 7135, Staffordshire, UK). This was achieved by transferring the cells onto coverslips pre-coated with Laminin at a concentration of 1 mg/mL, sourced from Sigma, Germany. A selection criterion based on fluorescence intensity was applied to choose cells for further investigation.

Electrophysiological data were gathered via the whole-cell configuration of the patch-clamp technique, employing Integrated Patch Clamp Amplifiers (Sutter Instruments, Novato, CA, USA) coupled with a Data Acquisition System from Sutter Instruments in Novato, CA. A piezoelectric translator from Automate Scientific in Berkeley, CA, which managed a dual-barrel theta glass pipette, expedited the exchange of solutions during the experiment. This setup facilitated the alternating application of an external wash solution and a test solution infused with essential oils derived from *A. judaica*, *P. oleracea*, and *Terminalia* chebula, with an added glutamate concentration of 10 mM. The composition of the external solution was 2.8 mM KCl, 150 mM NaCl, 2 mM $CaCl_2$, 0.5 mM $MgCl_2$, and 10 mM HEPES, neutralized to a pH of 7.4 using NaOH. The patch electrodes, crafted from borosilicate glass, were filled with a solution comprising 110 mM CsF, 30 mM CsCl, 4 mM NaCl, 0.5 mM $CaCl_2$, 10 mM EGTA, and 10 mM HEPES, with the pH adjusted to 7.2 using CsOH. The resistance of these electrodes was maintained within the range of 2–4 MΩ. The timing and rate of solution exchanges were precisely determined by evaluating junction potentials at the patch pipette's open tip post-recording, with a typical rise time between 200 and 300 microseconds (10–90%).

The deactivation and desensitization currents were elicited using a 10 mM glutamate application for 1 ms and 500 ms, respectively, under a holding potential of -60 mV, a pH of 7.4, and ambient room temperature conditions (20–23°C). These currents were recorded at a high sampling frequency of 10 kHz, with a low-pass filter set at 2

kHz to mitigate high-frequency noise, followed by digitization using SutterPatch Software v. 1.1.1 from Sutter Instruments.

Statistical Analysis

The antioxidant, anti-lipase, and anti-α-amylase of the three plants extract and positive controls were assessed, and the results are presented as the mean ± standard deviation (SD). Unpaired *t*-tests were used to compare the data. Statistical differences between the groups were examined by One Way ANOVA, with values of (*) $p < 0.05$, (**) $p < 0.01$, (***) $p < 0.001$ being considered to indicate statistical significance, ns, not significant. Concentration-response relationships were fitted as composite curves using GraphPad Prism version 6.01.

Results

Qualitative phytochemical screening tests

The crude aqueous extracts of the three studied medicinal plants revealed the presence of phytochemical compounds such as alkaloids, cardiac glycosides, phenols, tannins, and terpenoids, as presented in Table 1.

Table 1
Phytochemical screening tests for the aqueous extracts of each plant

Phytochemical Compounds	***Artemisia judaica***	***Portulaca oleracea***	***Terminalia chebula***
Alkaloids	-	-	-
Carbohydrates	-	-	-
Sugar	+	-	+
Cardiac Glycosides	-	-	+
Saponin	-	-	-
Phenols	+	+	+
Tannins	+	+	+
Flavonoids	+	+	+
Terpenoids	+	-	-
Protein	-	-	-

Quantitative analysis

Total phenols, flavonoids, and tannins were measured quantitatively, and their values are listed in Table 2. The quantities of important phytochemical classes in the three plant extracts varied significantly, according to the quantitative study. Out of all the extracts tested, *Terminalia chebula* was determined to have the highest phytochemical content. Compared to the other two extracts, its content of total phenols (1.633 mg GAE/g) was an order of magnitude higher, indicating significantly higher amounts of all tested chemicals. Additionally, it has the greatest concentrations of tannins (0.162 mg CAE/g) and flavonoids (0.294 mg RUE/g). The phytochemical

concentrations of *Portulaca oleracea* and *Artemisia judaica* were lower and more comparable. Of these two, *Artemisia judaica* had a slightly higher total phenol content (0.134 mg GAE/g), but *Portulaca oleracea* had the greatest flavonoid concentration (0.171 mg RUE/g).

Table 2
Total phenol, total flavonoid, and total tannin for each examined plant extract

Plant name	Total flavonoids contents, mg of RUE/g of dry extract ± standard deviation	Total phenol contents, mg of GAE/g of dry extract ± standard deviation	Total tannin contents, mg of CAE/g of dry extract ± standard deviation
Artemisia judaica	0.138	0.134	0.065
Portulaca oleracea	0.171	0.110	0.075
Terminalia chebula	0.294	1.633	0.162

Antioxidant activity

The free radical scavenging activity of *A. judaica*, *P. oleracea*, and *T. chebula* was assessed using DPPH, as shown in Fig. 1. Aqueous extracts from *Artemisia judaica*, *Terminalia chebula*, and *Portulaca oleracea* were tested for their in vitro antioxidant properties using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay. The findings showed that all three extracts have distinct antioxidant activity that varies with concentration. *Terminalia chebula* extract had the strongest radical scavenging ability, with the maximum percentage of inhibition across all tested doses, as predicted by the phytochemical quantification data. Its sharply rising dose-response curve suggested a low IC_{50} value, or the concentration needed to scavenge half of the DPPH radicals.

A dose-dependent inhibition of α-amylase was observed in all extracts (Table 3). With a considerable capacity to control the digestion of carbohydrates, *Terminalia chebula* was the most powerful inhibitor by a substantial margin (IC_{50} = 60.11 µg/mL). The activity of *Artemisia judaica* (IC_{50} = 441.38 µg/mL) and *Portulaca oleracea* (IC_{50} = 391.48 µg/mL) was significantly lower, but still detectable. As anticipated, the most potent inhibitor was the pharmaceutical medication acarbose (IC_{50} = 7.66 µg/mL).

Terminalia chebula's exceptionally showed low IC_{50} value of 13.64 µg/mL, which indicates a potent ability to scavenge free radicals, was validated by the antioxidant capacity experiment. *Portulaca oleracea* was the least effective (IC_{50} > 100 µg/mL), but *Artemisia judaica* exhibited moderate activity (IC_{50} = 69.57 µg/mL). As expected, the strongest antioxidant was the positive control, such as ascorbic acid.

Only *Terminalia chebula* showed significant efficacy in the pancreatic lipase inhibition experiment (IC_{50} = 468.52 µg/mL), indicating a potential to decrease the absorption of dietary fat. At the studied doses, *Artemisia judaica* and Portulaca oleracea were both essentially ineffective (IC_{50} > 1000 µg/mL). The conventional medication Orlistat (IC_{50} = 21.03 µg/mL) was significantly more effective than any natural extract.

Table 3
IC_{50} (µg/mL) values for each aqueous plant extract compared to control

	IC_{50} µg/mL			
Enzyme	*Artemisia judaica*	*Terminalis chebula*	*Portulaca oleracea*	Positive control
α -amylase	441.375 ± 0.99	60.1055 ± 0.49	391.4805 ± 3.48	7.66 ± 1.78 [a]
DPPH	69.571 ± 0.36	13.639 ± 0.12	> 100	0.545 ± 0.09[b]
Lipase	> 1000	468.52 ± 2.025	> 1000	21.025 ± 1.41[C]
[a] Acarbose, [b] Trolox, [C] Orlistate				

Antidiabetic activity by α-amylase inhibition assay for each plant extract

The antidiabetic activity of *A. judaica*, *P. oleracea*, and *T. chebula* was evaluated using the α-amylase inhibition assay, as shown in Fig. 2. The IC_{50} values are presented in Table 3 and compared with those of the positive control group.

Anti-obesity activity by lipase inhibition assay for each plant extract

The anti-obesity activity of *A. judaica*, *P. oleracea*, and *T. chebula* was evaluated using a lipase inhibition assay, as shown in Fig. 3. The IC_{50} values are presented in Table 3 and compared with those of the positive control group.

Antimicrobial testing

The antibacterial efficacy of aqueous extracts from *P. oleracea*, *A. judaica*, and *T. chebula* was evaluated using a micro-broth dilution method, as shown in Table 4. The results demonstrate a strong antibacterial effect of extracts from *A. judaica* and *T. chebula*. Specifically, *A. judaica* exhibited antimicrobial activity at 25 mg/ml concentrations against gram-positive bacterial strains (ATCC and clinical) and 50 mg/ml against gram-negative bacterial and fungal strains. Remarkably, *T. chebula* showed higher efficacy, with MIC values ranging from 1.56–6.25 mg/ml against the investigated bacterial strains and a MIC value of 0.78 mg/ml against the *C. albicans* strain.

Table 4
Antimicrobial activity minimal inhibitory concentration (MIC) values (mg/ml) of *Portulaca oleracea*, *Artemisia judaica* and *Terminalia chebula* aqueous extracts

	Bacteria						**Fungus**
	Gram-positive		**Gram-Negative**				**Yeast**
ATCC Number	Clinical strain	ATCC 25923	ATCC 25922	ATCC 13883	ATCC 8427	ATCC 9027	ATCC 90028
Microbe	MRSA	*Staphylococcus aureus*	*Escherichia coli*	*Klebsiella pneumoniae*	*Proteus vulgaris*	*Pseudomonas aeruginosa*	*Candida albicans*
Portulaca oleracea MIC (mg/ml)	R	R	R	R	R	R	R
Artemisia judaica MIC (mg/ml)	25	25	50	R	50	50	50
Terminalia chebula MIC (mg/ml)	1.56	1.56	3.125	3.125	3.125	6.25	0.78
R: Resistant							

Electrophysiological recordings for each extract against AMPA receptors

Antagonistic Effect of A. judaica, P. oleracae, and T. chebulla on AMPA receptor

The modulatory effects of *A. judaica, P. oleracae*, and *T. chebulla* on AMPA receptors were assessed using electrophysiological peak amplitude recordings. The recordings collected for each plant with GluA1, GluA1/2, GluA2, and GluA2/3 demonstrated an antagonistic relationship. *T. chebula* exhibited the strongest impact against GluA1, GluA1/2, GluA2, and GluA2/3 since it reduced AMPA receptor activity by 6.5, 7.2, 7.7, and 7-fold, respectively, as presented in Fig. 4e and 4f. *A. judaica* had the weakest impact. However, its impact was still significant at $p < 0.01$. This extract reduced AMPA receptor's activity, as depicted in Figs. 4a and 4b, by decreasing the A/A_I ratio (where A represents the current caused by glutamate alone, and A_I represent the current induced by glutamate + the plants extract) for each of the AMPA receptor configurations used (GluA1, GluA1/2, GluA2, and GluA2/3) by 3.5, 3.7, 3.9, and 3.6 times, respectively. Finally, the attenuation of AMPA receptors caused by *P. oleracae* extract was demonstrated through the significant decrease in inward current amplitude recorded using the whole-cell patch-clamp technique. The diminution was observed because *P. oleracae* affected each subunit by 4.9, 5, 5.3, and 4.9 times, respectively. All cells were exposed to glutamate alone after studying them against *A. judaica, P. oleracae*, and *T. chebulla* to ensure that the effects of the plants were not cytotoxic. All three of the plants reduced the activity of homologous GluA2 yet homologous GluA1 the least, suggesting a common mechanism behind their antagonism and providing valuable insights for their use in future research and treatments.

A. judaica, P. oleracae, and T. chebulla prolongs AMPA desensitization

Having established the antagonist effect of *A. judaica, P. oleracae*, and *T. chebulla* on AMPA receptor activity, we examined their influence on desensitization, a crucial regulatory mechanism in glutamatergic signalling. *T. chebula* exhibited the greatest reductive effect on desensitization rate (ms), decreasing the rate for GluA1, GluA2, and GluA2/3 from 3 to 4.3-fold, causing a prolonged desensitization time, which could contribute to glutamate build up and excitotoxicity (Fig. 5). *T. chebula* affected the GluA1/2 receptor by reducing it 1.8 times, but less significantly with $p < 0.01$, unlike its effect on the other subtypes with a significance of $p < 0.001$. *A. judaica* decreased the desensitization rate in GluA1, GluA1/2, GluA2, and GluA2/3 by 2, 1.2, 2.6, and 2.5-fold. Although significant, these results are lower than those obtained for *T. chebulla. P. oleracae* had a stronger effect than *A. judaica* but remained weaker than *T. chebulla* with desensitization reduction at 2.2, 1.3, 2.9, and 2.7 for each subtype used. The findings are depicted in Fig. 5.

A. judaica, P. oleracae, and T. chebulla accelerate AMPA deactivation

The deactivation rate was increased when *A. judaica, P. oleracae*, and *T. chebulla* were added, thus accelerating the process of deactivation, which enhances synaptic transmission and has a potential for excitotoxicity. In this part of the investigation, *T. chebula* exhibited the greatest effect on the rate of deactivation by increasing it 4, 3.5, 3.9, and 3.7-fold for GluA1, GluA1/2, GluA2, and GluA2/3, respectively (Fig. 6). This extract's effect was significant at $p < 0.001$. *P. oleracae* and *A. judaica* had similar potencies for the subunits; their results were significant at $p < 0.01$. *P. oleracae* had a slightly stronger effect because it accelerated deactivation by 2.9, 2.5, 2.9, and 2.7-fold for GluA1, GluA1/2, GluA2, and GluA2/3, respectively. *A. judaica* accelerated deactivation by 2.3 for GluA1 and GluA2 but 2-fold for GluA1/2 and GluA2/3.

Discussion

A wide range of secondary metabolites, such as alkaloids, terpenoids, phenolic compounds, and tannins, were identified by phytochemical characterization of aqueous extracts from *Artemisia judaica*, *Portulaca oleracea*, and *Terminalia chebula*. These metabolites are probably what give these plants their observed multi-target bioactivities. Notably, it was discovered that *Terminalia chebula* had a unique composition that included a wide range of main metabolites (proteins, carbs) and secondary metabolites, as well as cardiac glycosides. This abundance of phytochemicals supports a broader therapeutic potential in addition to being consistent with earlier screening investigations. Particularly noteworthy is the high concentration of flavonoids, tannins, and phenolic substances found in *T. chebula* extracts, which are highly correlated with the plant's noticeable in vitro bioactivity [45].

The antioxidant capacity of *T. chebula* was markedly evident in its DPPH scavenging activity, exhibiting an IC_{50} value that approximated that of Trolox, a standard antioxidant. This notable efficacy positions *T. chebula* as a leading antioxidant agent among the plants studied, with *A. judaica* displaying moderate activity and *P. oleracea* showing a more subdued effect. A previous study reported that aqueous extract of *T. chebula* was tested for antioxidant activity and effectively scavenged DPPH radicals, making it a potent antioxidant and a probable radioprotector [46]. In addition, another study evaluated the protective effects of *T. chebula* extract on tert-butyl hydroperoxide-induced oxidative injury in rat primary hepatocytes and liver. Suggesting that extract could prevent oxidative damage in living systems [47]. Moreover, *T. chebula* demonstrated a noteworthy activity against the α-amylase enzyme, inhibiting it with an IC_{50} value of 60.1055 ± 0.49 µg/mL, and its anti-lipase effects were also significant, albeit moderate, with an IC_{50} value of 468.52 ± 2.025 µg/mL, indicating a broader spectrum of

bioactivity that may have implications for metabolic health. In contrast, *Artemisia judaica* and *Portulaca oleracea* exhibited lesser effects on these enzymes, with α-amylase inhibition IC_{50} values of 441.375 ± 0.99 µg/mL and 391.4805 ± 3.48 µg/mL respectively, and both showing negligible lipase inhibition (IC_{50} > 1000 µg/mL), highlighting the distinctive bioactive profile of *T. chebula*.

In the realm of antimicrobial efficacy, *T. chebula* emerged as a formidable contender, exhibiting pronounced inhibitory actions against a wide array of microbial adversaries, including the notorious MRSA and *Staphylococcus aureus*, as well as demonstrating significant antifungal prowess against *Candida albicans*. This spectrum of antimicrobial activity underscores *Terminalia chebula's* robust bioactive arsenal and aligns seamlessly with documented research, reinforcing its esteemed position in the pantheon of medicinal plants with potent antimicrobial properties [48]. The compelling evidence of its broad-spectrum efficacy, particularly against pathogens of high clinical relevance, positions *T. chebula* as a pivotal resource for developing novel antimicrobial agents, heralding a new era in the fight against resistant microbial strains. Meanwhile, *A. judaica* and *P. oleracea*, though demonstrating more modest antimicrobial effects, contribute to the collective therapeutic landscape, highlighting the diverse antimicrobial strategies nature offers through these botanicals. This intricate interplay of antimicrobial activities enriches these plants' pharmacological tapestry and underscores the intricate balance between their traditional uses and potential modern applications in combating microbial threats [49].

The transition from these botanicals' traditional antimicrobial and antioxidant roles to their neuropharmacological impact provides a deeper understanding of their therapeutic potential. The potent effects of *T. chebulam, A. judaica*, and *P. oleracea's* moderate activities extend beyond their primary biochemical interactions, influencing crucial neural pathways and receptor dynamics. The modulation of AMPA receptor activity by these plant extracts, characterized by significant inhibitory effects and adjustments in receptor kinetics, echoes the complex interplay between their established bioactive profiles and their emerging neuroprotective and cognitive-enhancing roles. This convergence of traditional phytochemical attributes with modern neuropharmacological insights enriches the narrative surrounding these plants, advancing our comprehension of their mechanisms and reinforcing their potential for neurotherapeutic development.

A. judaica, with its pronounced antioxidant, anti-inflammatory, and neuromodulatory properties, as demonstrated in studies involving diabetic rat models, revealed a potential mechanism that mirrors the AMPA receptor modulation observed in our experiments. Such mechanism, characterized by a reduction in excitotoxicity and an overall neuroprotective stance, suggests *A. judaica's* broader applicability in mitigating the neuronal impacts of systemic metabolic anomalies [50]. In the case of *P. oleracea*, the link between its antidepressant-like properties and AMPA receptor modulation provides a fresh perspective on its neuropharmacological profile. The significant behavioral changes, such as reduced immobility in depressive-like states attenuated by AMPA receptor antagonism, highlight the extract's role in mood regulation and cognitive functions. This interplay with AMPA receptors suggests a complex mechanism where *P. oleracea* combats oxidative stress and fine-tunes neurotransmitter receptor dynamics, reinforcing its potential in neurodegenerative and cognitive disorder therapeutics [51]. *T. chebula's* role, particularly its acetylcholinesterase inhibitory and antioxidant activities, offers a dual pathway for combating neurodegenerative processes, especially those akin to Alzheimer's. The ability to enhance cholinergic transmission while simultaneously modulating glutamatergic signaling through AMPA receptors underlines a holistic approach to neuroprotection, suggesting *T. chebula's* utility extends beyond Alzheimer's to encompass a wide range of neurological conditions [52]. Together, the intertwined effects of these botanicals, from receptor-specific interactions to broad systemic neuroprotection, underscore a complex yet

promising landscape of neuropharmacological research. The alignment of our findings with those from individual plant studies advocates for a deeper exploration into the multifaceted roles these extracts play in neurotherapy, highlighting the critical importance of botanicals in the ongoing search for effective treatments against neurological disorders.

The culmination of this investigation into *A. judaica*, *P. oleracea*, and *T. chebula* broaden our scientific understanding of their phytochemical spectra and underscore the critical importance of integrating botanical knowledge into contemporary pharmacological research. The detailed elucidation of their diverse bioactive compounds, from antioxidative to neuroprotective properties, highlights a promising avenue for developing novel therapeutics. This study reinforces the concept that natural products remain an invaluable reservoir of pharmacologically active agents, urging a deeper, more nuanced exploration of plant-based compounds in the context of drug discovery and development. As we advance the frontier of neuropharmacology, the insights gleaned from the modulation of AMPA receptor dynamics by these botanical extracts provide a compelling narrative for their potential roles in addressing complex neurological disorders. The convergence of traditional phytochemical attributes with modern neuropharmacological mechanisms invites a multidisciplinary research approach that harmonizes botanical sciences with molecular pharmacology. This integrated perspective enriches our scientific repertoire and paves the way for more targeted, effective therapeutic strategies, embodying the essence of translational science in bridging the gap between benchtop discoveries and clinical applications. In this light, the study serves as a foundational pillar, advocating for a more collaborative, cross-disciplinary exploration of the medicinal potential of the plant kingdom, thereby contributing to the broader scientific endeavor of enhancing human health through the power of nature's medicine chest.

Conclusion

The results of this study show that the chosen medicinal herbs, Artemisia judaica, Terminalia chebula, and Portulaca oleracea, have significant multi-target pharmacological activity that support their traditional medicinal use. High concentrations of phenolic components, flavonoids, and tannins were confirmed by phytochemical analysis; among the studied extracts, T. chebula exhibited the highest concentration of bioactive ingredients. The highest antioxidant activity was consistently shown by T. chebula, which also showed significant α-amylase inhibition and moderate pancreatic lipase inhibition, suggesting promising anti-diabetic and anti-obesity potential.

Furthermore, T. chebula and A. judaica had broad-spectrum efficacy against both Gram-positive and Gram-negative bacteria as well as Candida albicans, demonstrating their potential as natural antimicrobial agents, according to the antimicrobial assays. All of these results point to T. chebula in particular as a potential source of bioactive substances with antibacterial, antioxidant, and neuroprotective properties. The study's multi-target biological activities encourage more research into these plant extracts as supplemental or alternative therapeutic agents for the treatment of metabolic, microbial, and oxidative stress-related illnesses.

This study has a number of limitations that should be noted despite the encouraging results. Initially, every biological assessment was carried out in vitro, which might not accurately represent the intricacy of biological reactions in in vivo settings. Therefore, care should be taken when extrapolating these findings to clinical or physiological applications. Moreover, although quantifying the phytochemical composition, the study failed to separate or pinpoint the specific active substances in charge of the biological activities that were detected. To gain a better understanding of the precise mechanisms of action, future research combining compound purification and mechanistic analyses is required.

Declarations

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Contributions

Conceptualization, M.Q., and B.R; methodology, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M.; software, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., and S.B; validation, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M.; formal analysis, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M.; investigation, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., and S.A.; resources, N.J.; data curation, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M., and S.M; writing—original draft preparation, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M.; writing—review and editing, M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M.; visualization, F M.Q., B.R., N.J., M.H., M.Q, S.R., Y.F., N.B., S.B., M.B., S.A., and S.M.; supervision, M.Q., B.R., N.J., and M.H.; project administration, F M.Q., B.R., N.J., and M.H.; funding acquisition, M.Q., B.R., N.J., and M.H.

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Ethics declarations

Ethics approval and consent to participate

Not Applicable.

Consent for publication

Not Applicable.

Competing interests

Not Applicable.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

References

1. Saboon, Chaudhari SK, Arshad S, Amjad MS, Akhtar MSJNB-aCVP, Applications. Natural compounds extracted from medicinal plants and their applications. 2019:193-207.
2. Radhika Baheti DT, Jayashri Mahore, Rashmi Trivedi, and Vinita Patole. Phytochemicals and Medicinal Plants: A Promising Frontier for Antiviral Research in the Age of Pandemics: REVIEW. Palestinian Medical and Pharmaceutical Journal. 2024;9(3).
3. Dalamaga M, Kounatidis D, Tsilingiris D, Vallianou NG, Karampela I, Psallida S, et al. The Role of Endocrine Disruptors Bisphenols and Phthalates in Obesity: Current Evidence, Perspectives and Controversies. International Journal of Molecular Sciences. 2024;25(1):675.
4. Al-Nimer M. Barriers to Diabetes Care during Humanitarian Crisis during 2013–2022 in Five Arabian Countries: A Systematic Review. Clinical Diabetology. 2023;12(2):123-34.
5. Chaudhary MR, Chaudhary S, Sharma Y, Singh TA, Mishra AK, Sharma S, et al. Aging, oxidative stress and degenerative diseases: mechanisms, complications and emerging therapeutic strategies. Biogerontology. 2023;24(5):609-62.
6. Chen X, Guo C, Kong J. Oxidative stress in neurodegenerative diseases. Neural regeneration research. 2012;7(5):376-85.
7. Sofowora A, Ogunbodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. African journal of traditional, complementary, and alternative medicines : AJTCAM. 2013;10(5):210-29.
8. Revett TJ, Baker GB, Jhamandas J, Kar S. Glutamate system, amyloid ß peptides and tau protein: functional interrelationships and relevance to Alzheimer disease pathology. Journal of psychiatry & neuroscience : JPN. 2013;38(1):6-23.
9. Pang ZP, Han W. Regulation of synaptic functions in central nervous system by endocrine hormones and the maintenance of energy homoeostasis. Bioscience reports. 2012;32(5):423-32.
10. Qneibi M, Bdir S, Maayeh C, Bdair M, Sandouka D, Basit D, et al. A Comprehensive Review of Essential Oils and Their Pharmacological Activities in Neurological Disorders: Exploring Neuroprotective Potential. Neurochemical research. 2023.
11. Herguedas B, García-Nafría J, Cais O, Fernández-Leiro R, Krieger J, Ho H, et al. Structure and organization of heteromeric AMPA-type glutamate receptors. Science. 2016;352(6285):aad3873.
12. Whitehead G, Regan P, Whitcomb DJ, Cho K. Ca(2+)-permeable AMPA receptor: A new perspective on amyloid-beta mediated pathophysiology of Alzheimer's disease. Neuropharmacology. 2017;112(Pt A):221-7.
13. Hansen KB, Wollmuth LP, Bowie D, Furukawa H, Menniti FS, Sobolevsky AI, et al. Structure, Function, and Pharmacology of Glutamate Receptor Ion Channels. Pharmacol Rev. 2021;73(4):298-487.

14. Tanaka H, Grooms SY, Bennett MV, Zukin RS. The AMPAR subunit GluR2: still front and center-stage. Brain Res. 2000;886(1-2):190-207.
15. Moharram FA, Nagy MM, El Dib RA, El-Tantawy MM, El Hossary GG, El-Hosari DG. Pharmacological activity and flavonoids constituents of Artemisia judaica L aerial parts. Journal of ethnopharmacology. 2021;270:113777.
16. Liu C, Murch S, El-Demerdash M, Saxena P. Artemisia judaica L.: micropropagation and antioxidant activity. Journal of Biotechnology. 2004;110(1):63-71.
17. El-Massry KF, El-Ghorab AH, Farouk A. Antioxidant activity and volatile components of Egyptian Artemisia judaica L. Food chemistry. 2002;79(3):331-6.
18. Lim YY, Quah EP. Antioxidant properties of different cultivars of Portulaca oleracea. Food chemistry. 2007;103(3):734-40.
19. Uddin MK, Juraimi AS, Ali ME, Ismail MR. Evaluation of antioxidant properties and mineral composition of purslane (Portulaca oleracea L.) at different growth stages. International journal of molecular sciences. 2012;13(8):10257-67.
20. Xiang L, Xing D, Wang W, Wang R, Ding Y, Du L. Alkaloids from Portulaca oleracea L. Phytochemistry. 2005;66(21):2595-601.
21. Tian J-L, Liang X, Gao P-Y, Li D-Q, Sun Q, Li L-Z, et al. Two new alkaloids from Portulaca oleracea and their cytotoxic activities. Journal of Asian natural products research. 2014;16(3):259-64.
22. AE AM. The neuroprotective effects of purslane (Portulaca oleracea) on rotenone-induced biochemical changes and apoptosis in brain of rat. CNS & Neurological Disorders Drug Targets. 2013;12(6):830-41.
23. P S. Anti-Diabetic Potential of Therapeutic Medicinal Plants: A Review. Palestinian Medical and Pharmaceutical Journal. 2024;9(3).
24. Kim HL, Choi B-K, Yang SH. Terminalia chebula Medicinal Uses: A Review of in vitro and in vivo Studies. Biotechnology and Bioprocess Engineering. 2022;27(5):729-39.
25. Gupta PC. Biological and pharmacological properties of Terminalia chebula Retz.(Haritaki)-An overview. Int J pharm pharm Sci. 2012;4(3):62-8.
26. Bag A, Bhattacharyya SK, Chattopadhyay RR. The development of Terminalia chebula Retz.(Combretaceae) in clinical research. Asian Pacific journal of tropical biomedicine. 2013;3(3):244-52.
27. Wang L, Weller CL. Recent advances in extraction of nutraceuticals from plants. Trends in Food Science & Technology. 2006;17(6):300-12.
28. Shaikh JR, Patil M. Qualitative tests for preliminary phytochemical screening: An overview. International Journal of Chemical Studies. 2020;8(2):603-8.
29. Gracelin DHS, Britto A, Kumar B. Qualitative and quantitative analysis of phytochemicals in five Pteris species. Int J Pharm Pharm Sci. 2013;5(1):105-7.
30. Santhi K, Sengottuvel R. Qualitative and quantitative phytochemical analysis of Moringa concanensis Nimmo. International Journal of Current Microbiology and Applied Sciences. 2016;5(1):633-40.
31. Gurupriya S, Cathrine L, Ramesh J. Qualitative and quantitative phytochemical analysis of Simarouba glauca leaf extract. Int J Res Appl Sci Eng Technol. 2017;5(11):475-9.
32. Maurya S, Singh D. Quantitative analysis of total phenolic content in Adhatoda vasica Nees extracts. International Journal of PharmTech Research. 2010;2(4):2403-6.

33. Crozier A, Lean ME, McDonald MS, Black C. Quantitative analysis of the flavonoid content of commercial tomatoes, onions, lettuce, and celery. Journal of agricultural and food chemistry. 1997;45(3):590-5.
34. Bustanji Y, Issa A, Mohammad M, Hudaib M, Tawah K, Alkhatib H, et al. Inhibition of hormone sensitive lipase and pancreatic lipase by Rosmarinus officinalis extract and selected phenolic constituents. Journal of Medicinal Plants Research. 2010;4(21):2235-42.
35. Zheng C-D, Duan Y-Q, Gao J-M, Ruan Z-G. Screening for anti-lipase properties of 37 traditional Chinese medicinal herbs. Journal of the Chinese Medical Association. 2010;73(6):319-24.
36. Ali H, Houghton P, Soumyanath A. α-Amylase inhibitory activity of some Malaysian plants used to treat diabetes; with particular reference to Phyllanthus amarus. Journal of ethnopharmacology. 2006;107(3):449-55.
37. Jaradat NA, Abualhasan M. Comparison of phytoconstituents, total phenol contents and free radical scavenging capacities between four Arum species from Jerusalem and Bethlehem. Pharmaceutical Sciences. 2016;22(2):120.
38. Jaradat N, Khasati A, Hawi M, Hawash M, Shekfeh S, Qneibi M, et al. Antidiabetic, antioxidant, and anti-obesity effects of phenylthio-ethyl benzoate derivatives, and molecular docking study regarding α-amylase enzyme. Scientific Reports. 2022;12(1):3108.
39. Jaradat N, Qadi M, Ali I, Hussein F, Issa L, Rashdan D, et al. Phytochemical screening, antiobesity, antidiabetic and antimicrobial assessments of Orobanche aegyptiaca from Palestine. BMC Complementary Medicine and Therapies. 2021;21(1):256.
40. Qadi M, Jaradat N, Al-lahham S, Ali I, Abualhasan MN, Shraim N, et al. Antibacterial, Anticandidal, Phytochemical, and Biological Evaluations of Pellitory Plant. BioMed Research International. 2020;2020:6965306.
41. Balouiri M, Sadiki M, Ibnsouda SK. Methods for in vitro evaluating antimicrobial activity: A review. J Pharm Anal. 2016;6(2):71-9.
42. Qneibi M, Hamed O, Fares O, Jaradat N, Natsheh A-R, AbuHasan Q, et al. The inhibitory role of curcumin derivatives on AMPA receptor subunits and their effect on the gating biophysical properties. European Journal of Pharmaceutical Sciences. 2019;136:104951.
43. Qneibi M, Hamed O, Natsheh A-R, Fares O, Jaradat N, Emwas N, et al. Inhibition and assessment of the biophysical gating properties of GluA2 and GluA2/A3 AMPA receptors using curcumin derivatives. Plos one. 2019;14(8):e0221132.
44. Qneibi M, Hamed O, Jaradat N, Hawash M, Al-Kerm R, Al-Kerm R, et al. The AMPA receptor biophysical gating properties and binding site: Focus on novel curcumin-based diazepines as non-competitive antagonists. Bioorganic Chemistry. 2021;116:105406.
45. Vemuri PK, Dronavalli L, Nayakudugari P, Kunta A, Challagulla R. Phytochemical analysis and biochemical characterization f terminalia chebula extracts for its medicinal use. Biomedical and Pharmacology Journal. 2019;12(3):1525-9.
46. Naik G, Priyadarsini K, Naik D, Gangabhagirathi R, Mohan H. Studies on the aqueous extract of Terminalia chebula as a potent antioxidant and a probable radioprotector. Phytomedicine. 2004;11(6):530-8.
47. Lee H-S, Won NH, Kim KH, Lee H, Jun W, Lee K-W. Antioxidant effects of aqueous extract of Terminalia chebula in vivo and in vitro. Biological and Pharmaceutical Bulletin. 2005;28(9):1639-44.

48. Jinukuti MG, Giri A. Antimicrobial activity of aqueous extract of Terminalia chebula Retz. Proteus. 2013;30:0.35.
49. Deepak S, Kamat S, Kamat D. Effect of aqueous extract of Terminalia chebula on metallo beta lactamase. International Journal of Pharmacy and Pharmaceutical Sciences. 2010;2(4):172-5.
50. Albasher G, Aljarba N, Al Sultan N, Alqahtani WS, Alkahtani S. Evaluation of the neuro-protective effect of Artemisia judaica extract in a murine diabetic model. Journal of Food Biochemistry. 2020;44(8):e13337.
51. Park S-J, Choi M-J, Chung S-Y, Kim J-W, Cho S-H. The involvement of AMPA receptor in the antidepressant-like effects of the portulaca oleracea L. extract in mice. Journal of Oriental Neuropsychiatry. 2013;24(3):271-80.
52. Afshari AR, Sadeghnia HR, Mollazadeh H. A review on potential mechanisms of Terminalia chebula in Alzheimer's disease. Advances in Pharmacological and Pharmaceutical Sciences. 2016;2016.

Figures

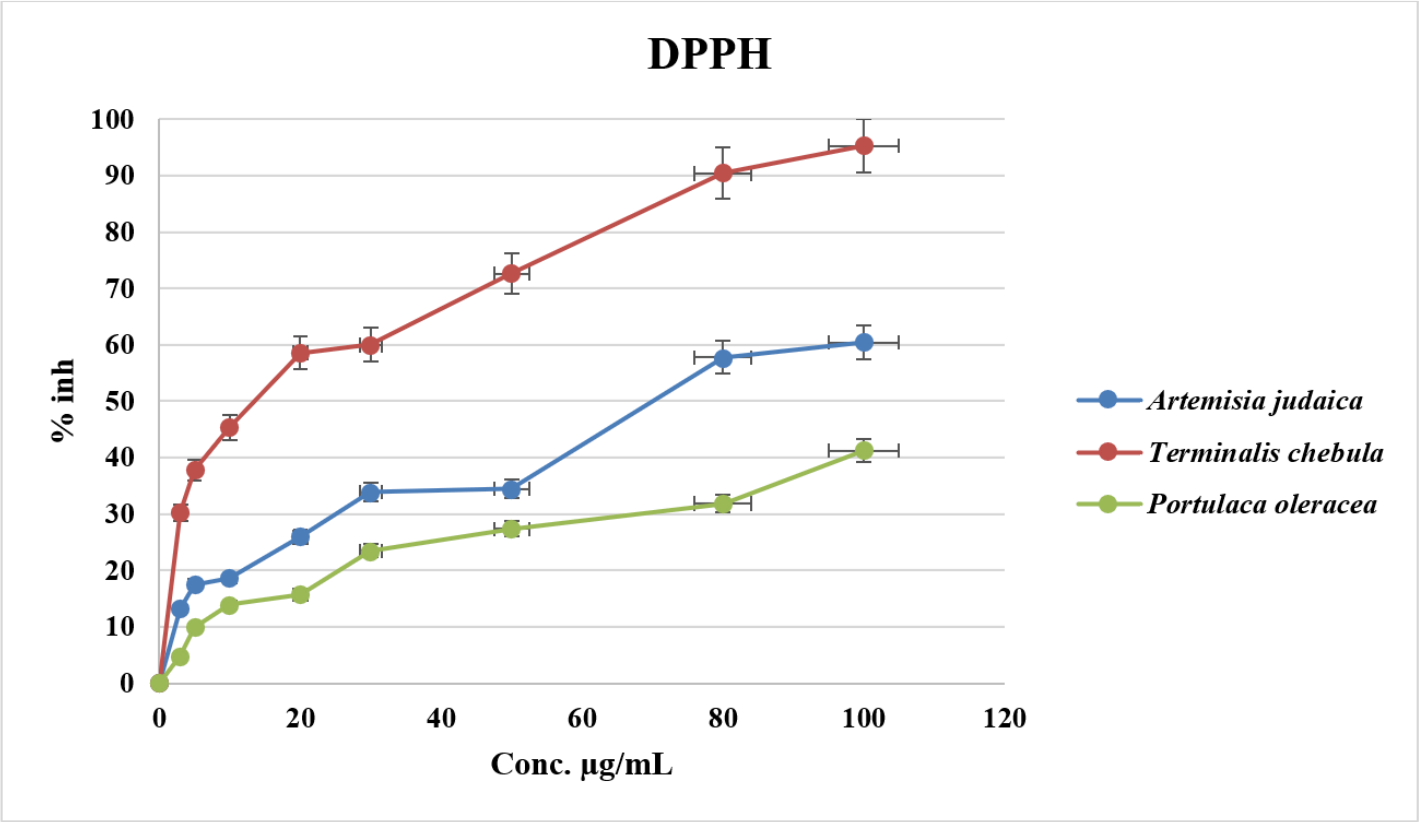

Figure 1

DPPH inhibitory activity by each aqueous plant extract

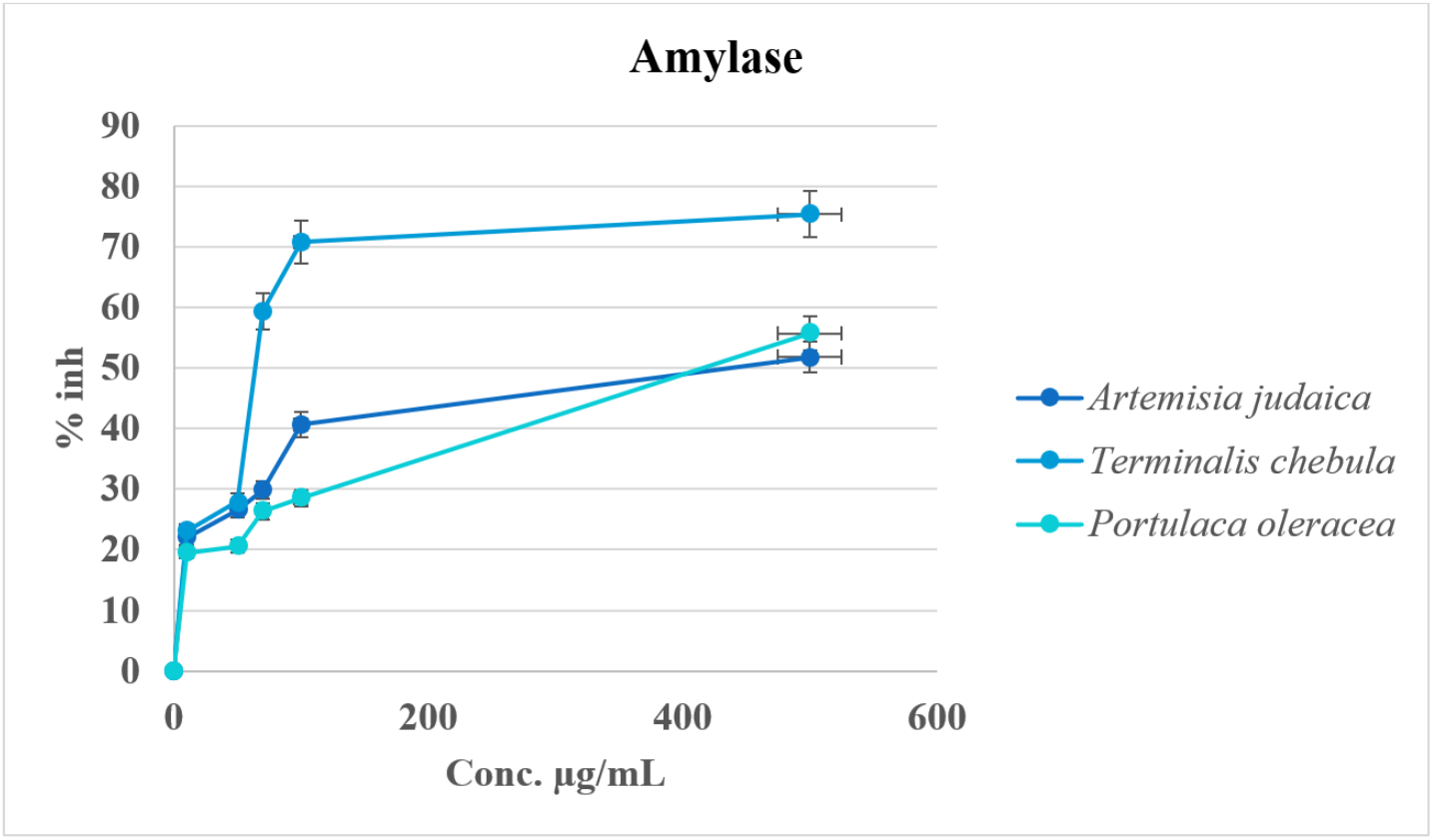

Figure 2

α- amylase inhibition activity by each aqueous plant extract

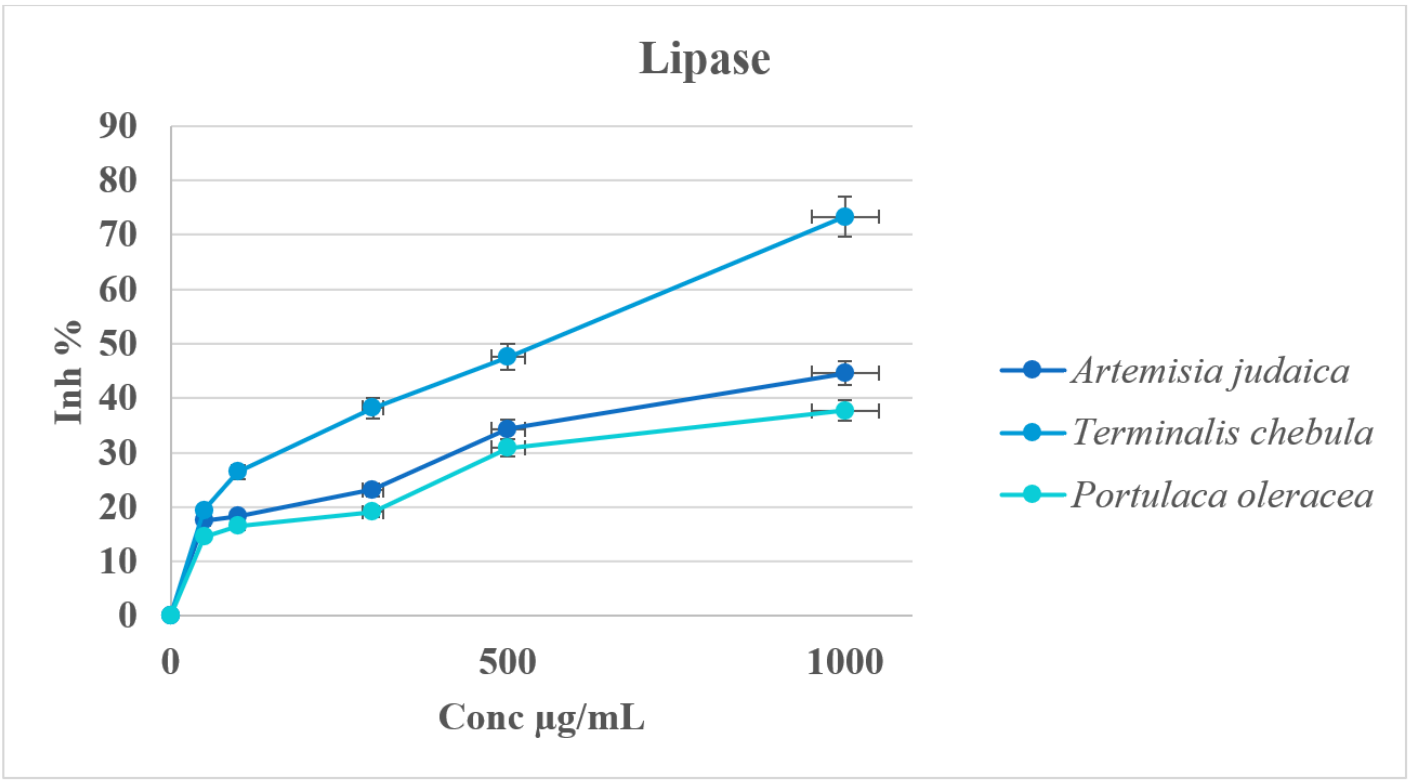

Figure 3

Lipase inhibition activity by each aqueous plant extract

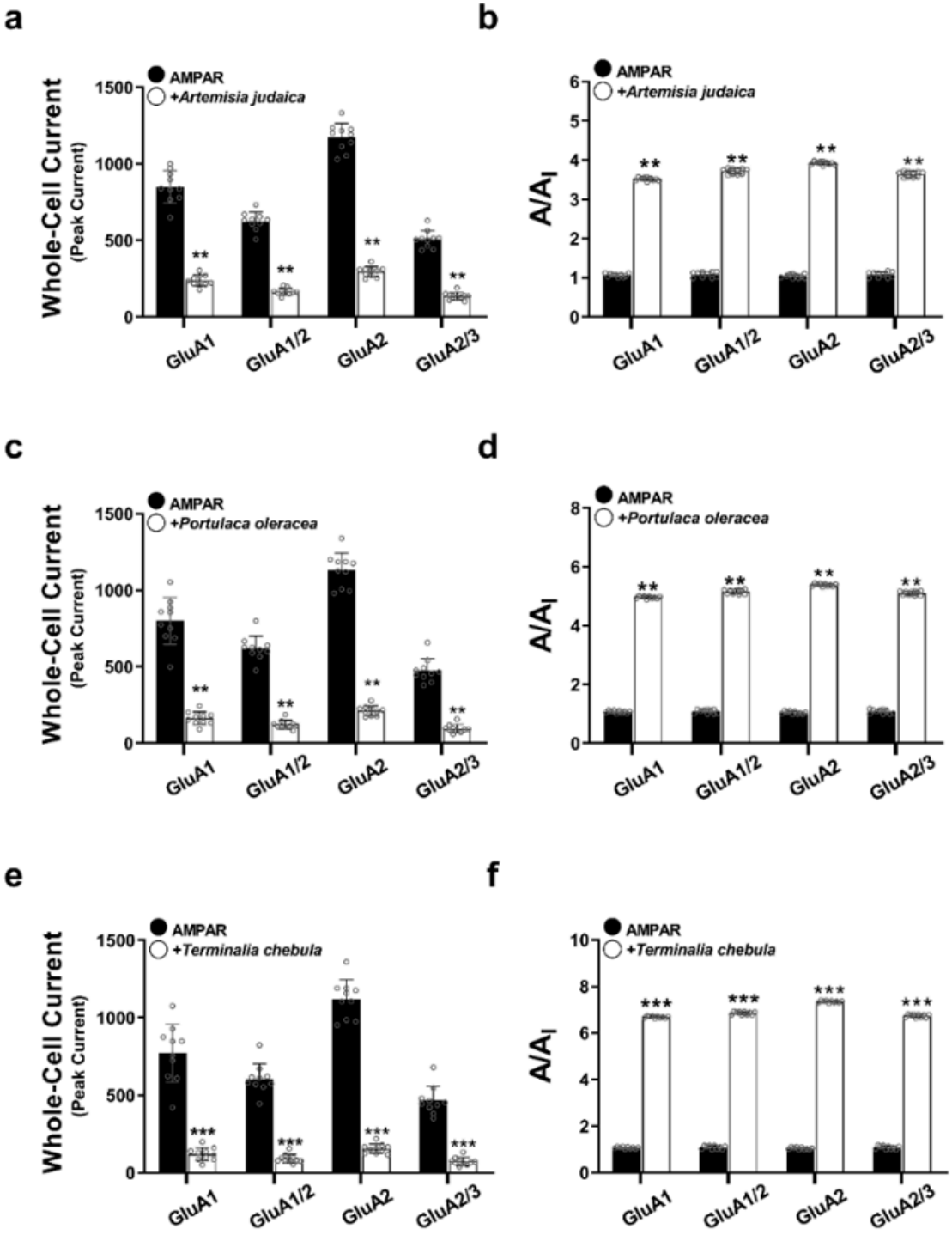

Figure 4

Modulation of AMPA Receptor Currents by *A. judaica, P. oleracae, and T. chebulla* Extracts. Whole-cell patch-clamp recordings of peak inward currents evoked by AMPA application in HEK293T cells expressing GluA1, GluA1/2,

GluA2, and GluA2/3 AMPA receptor subtypes. The currents elicited by AMPA receptors treated with *A. judaica*, *P. oleracae*, and *T. chebulla*, respectively (labeled as white), are compared to the currents generated by untreated receptors (labelled as black), as shown in a, c, and e. The A/A_I ratios for *A. judaica*, *P. oleracae*, and T. *chebulla* are shown by b, d, and f, respectively. A one-way analysis of variance (ANOVA) was used to do statistical analysis to evaluate disparities.: *p < 0.05; **p < 0.01; ***p < 0.001; ns, not significant. The number of cells assessed for each condition (n = 10). Data are represented as mean ± standard error of the mean (SEM).

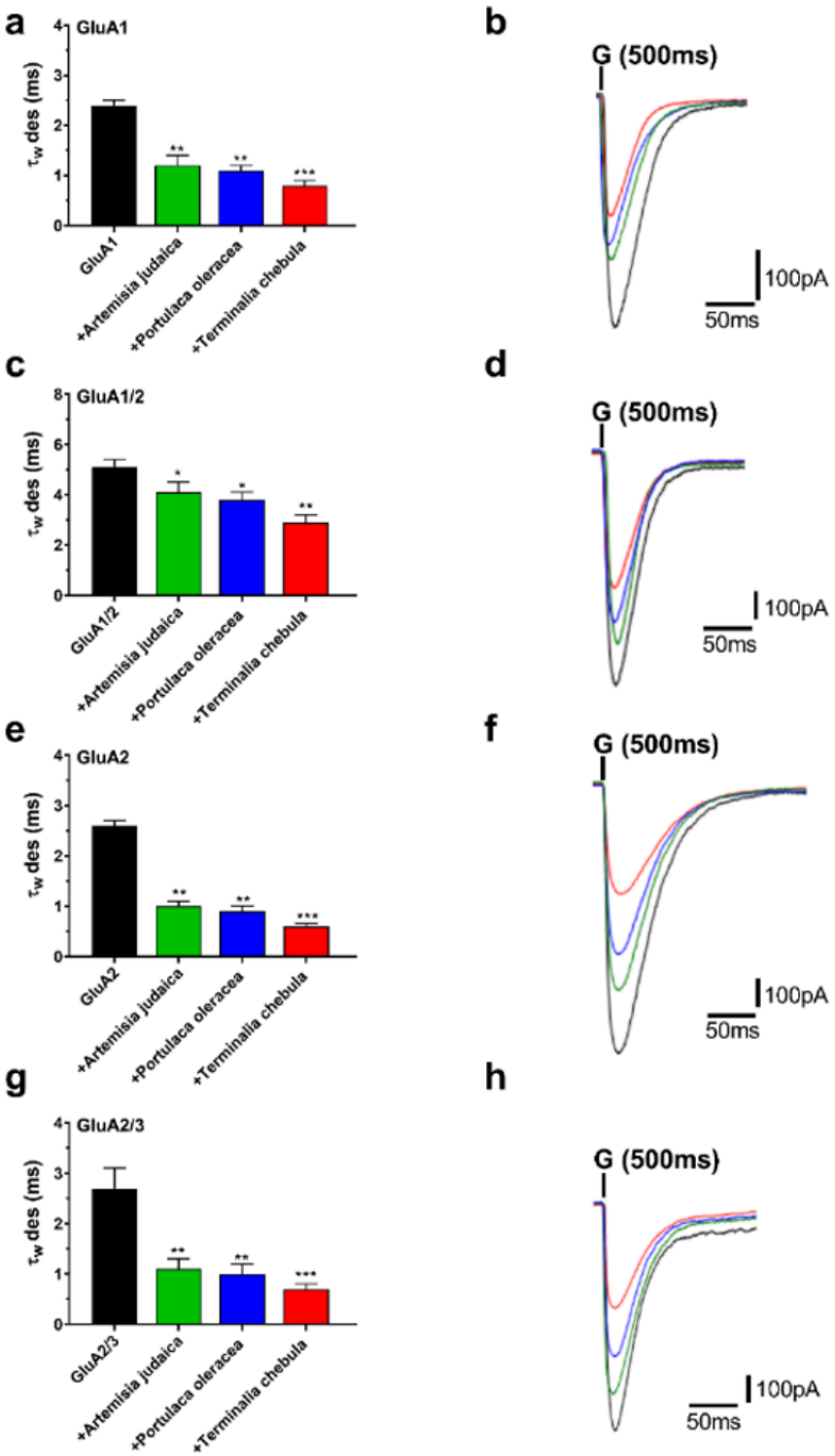

Figure 5

Desensitization Rate of AMPA receptor subunits after using *A. judaica, P. oleracae,* and *T. chebulla.* The desensitization rates for GluA1 (a), GluA1/2 (c), GluA2 (e), and GluA2/3 (g) are compared in Figures (a, c, e, and g) in black, with the rate seen following treatment with *A. judaica* (green), *P. oleracae* (blue), and *T. chebulla* (red). The comparative examination of the receptor's subtypes with each extract is shown in Figures (b, d, f, h). The time per recording is set at 500 ms after 10mM application is given at -60 mV, a pH of 7.4, and temperature (20-23 °C). Statistical analysis was conducted using ANOVA to assess differences: *p < 0.05; **p < 0.01; ***p < 0.001; ns, not significant. The number of cells evaluated for each condition (n = 10). Data are represented as mean ± SEM.

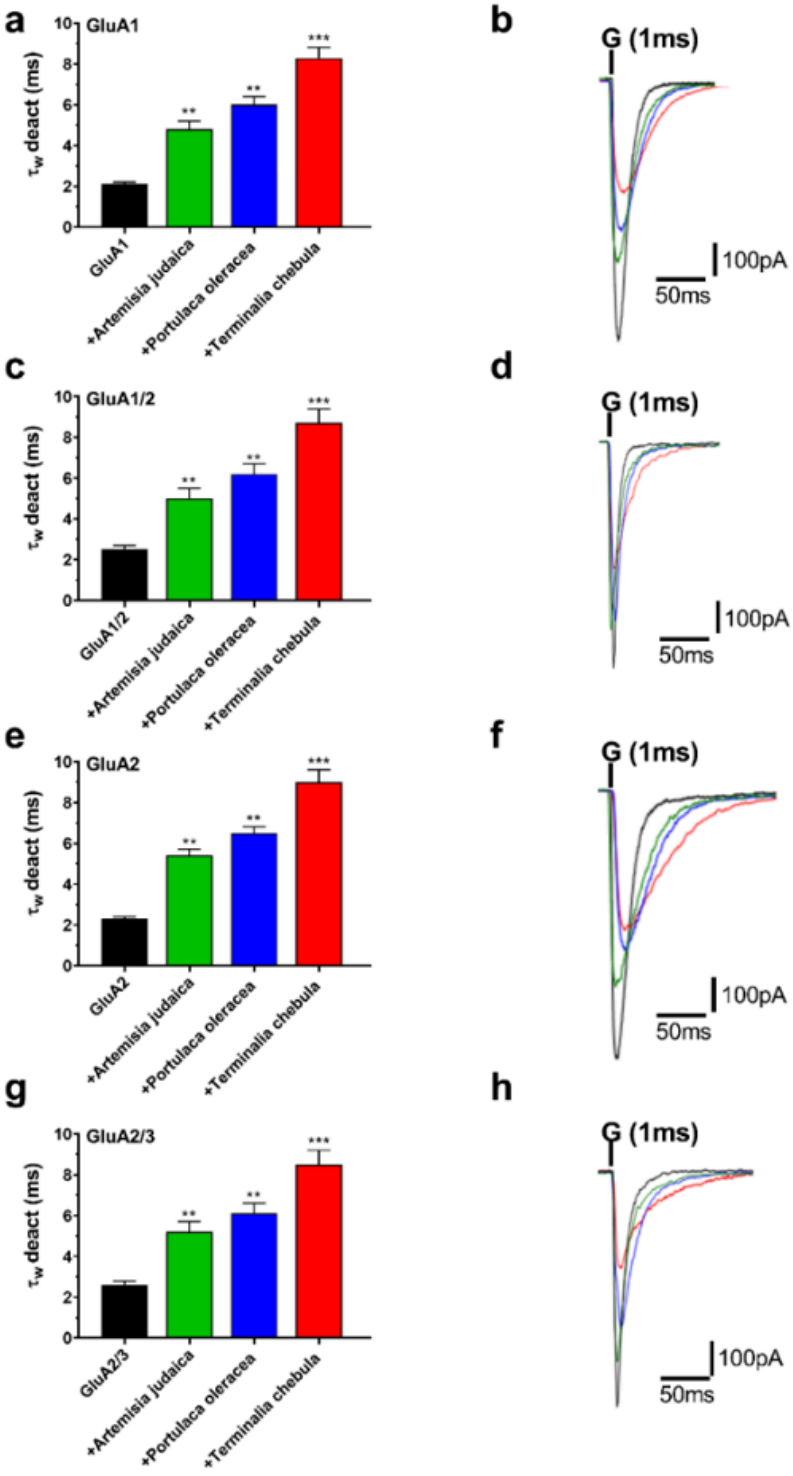

Figure 6

Deactivation Rate of AMPA receptor subunits after using *A. judaica, P. oleracae,* and *T. chebulla.* The deactivation rates for GluA1 (a), GluA1/2 (c), GluA2 (e), and GluA2/3 (g) are compared in figures (a, c, e, and g) in black. The comparison is made with the rate following treatment with *A. judaica* (green), *P. oleracae* (blue), and *T. chebulla* (red). The comparative examination of the receptor's subtypes with each extract is shown in Figures (b, d, f, h). The time per recording is set at 50 ms after 10 mM application is given at -60 mV, a pH of 7.4, and temperature (20-23 °C). Statistical analysis was conducted using ANOVA to assess differences: *p < 0.05; **p < 0.01; ***p < 0.001; ns, not significant. The number of cells evaluated for each condition (n = 10). Data are represented as mean ± SEM.

Supplementary Files

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- SupplementaryMaterial1.docx