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Original Research

Alpha-Mangostin Attenuates Oxidative Stress and Apoptosis in Scopolamine-Induced Amnesic Rat Brains

Suksan Changlek[1,2], Rungrudee Srisawat[1]*

[1]*School of Preclinical Sciences, Institute of Science, Suranaree University of Technology, Nakhon Ratchasima, Thailand*
[2]*School of Allied Health Sciences, Walailak University, Nakhon Si Thammarat, Thailand*

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Abstract

The extract from *Garcinia mangostana* L. pericarp was reported to scavenge radicals, inhibit acetylcholinesterase (AChE) activity, and improve spatial memory in scopolamine (SCOP)-induced amnesic rats. This study investigated α-mangostin (α-MG) neuroprotective effects against SCOP-induced neurotoxicity.The compound was evaluated for anti-AChE and antioxidant properties *in vitro*, and its preventive effect on apoptosis and oxidative stress in SCOP-treated rat brains. AChE inhibitory property of α-MG was assessed by fast blue B (FB) salt and β-naphthyl acetate (NA) and Ellman's assays. The antioxidant properties of α-MG were assessed by ferric reducing antioxidant power (FRAP), scavenging activity of 1,1-diphenyl-2-picrylhydrazyl (DPPH), and 2,2′-azino-bis-[3-ethylbenzothiazoline-6-sulfonic acid] ($ABTS^{\bullet+}$) radicals. Brain levels of malondialdehyde (MDA), lipid peroxidation marker, and activities of the caspase-3 enzyme, an apoptosis-related marker, were determined in SCOP-treated rats pretreated with donepezil (DPZ) and α-MG. IC50 of α-MG and DPZ for AChE activity were 64.23±0.22 and 32.46±0.14 mg/mL, respectively. α-MG and DPZ (100-600 µg/mL) gave FRAP values within the range of 20-410 µmol Fe^{2+}/L. The IC_{50} of α-MG and DPZ for ABTS were 21.52±3.45 and 14.53±1.86 µg/mL, and for DPPH were 38.12±8.36 and 29.44±5.13 µg/mL, respectively. Prior given to SCOP-induced rats, DPZ and α-MG (50 and 100 mg/kg) reduced MDA levels, and pretreatment of DPZ and α-MG (50 mg/kg), but not α-MG (100 mg/kg), attenuated the increase of caspase-3 activity in cerebral cortex and hippocampus ($P<0.05$), but not in the basal forebrain. The present study is the first report of α-MG as a potential neuroprotective candidate, and its mechanism might be involved in ameliorating scopolamine-induced neurotoxicity *via* inhibition of lipid peroxidation and caspase-3 enzyme activity in the cerebral cortex and hippocampus.

Keywords: Alpha-mangostin; Acetylcholinesterase; Apoptosis; Caspase-3; Lipid peroxidation; Cerebral cortex; Hippocampus

Introduction

Alzheimer's Disease (AD) is a dangerous disease with a significant loss of memory and cognitive and behavioral disturbances as the etiological features [1-4]. In general, acetylcholinesterase (AChE), a serine hydrolase is primarily related to cholinergic neurons that catalyzes the hydrolysis of acetylcholine (ACh). AChE is highly efficient since more than 10,000 molecules of acetylcholine are cleaved promptly [5]. AChE inhibitors increase the neurotransmission of ACh by providing relief and improving the behavior of AD patients, but none can restore or reverse the progress of AD [6]. Therefore, antioxidants have been recommended in therapies to protect, prolong or alleviate the underlying causes of AD progress [7-8]. The apoptotic process is induced by oxidative stress *via*

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*Corresponding Author: Rungrudee Srisawat
School of Preclinical Sciences, Institute of Sciences, Suranaree University of Technology, Nakhon Ratchasima, Thailand
Email: srisawat@sut.ac.th

the generation of singlet oxygen [9]. Recently, the antioxidants found in natural compounds have attracted attention, which are candidates to prevent oxidative damage [10-12]. Many polyphenols from plants have represented neuroprotective mechanisms against AD [13].

The fruit rind of *Garcinia mangostana* L. is traditionally described to treat diarrhea, skin wounds, and infection. Several types of xanthones were found in the fruit rind of *G. mangostana*. A previous study has indicated that *G. mangostana* has a scavenging activity of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical. A preliminary study found that the aqueous/ethanol extract from the fruit rind of *G. mangostana* showed memory enhancing and AChE inhibiting activities in normal mature and normal-aged rats [14-16]. Although *G. mangostana* demonstrates its anti-AD ability, which has important pharmacological value for AD treatment, there has not been any study yet evaluating the phenolic core structure. Hence, the aim of the present study is to examine the neuroprotective effects against SCOP neurotoxicity of α-mangostin (α-MG), a natural product containing xanthone core structure isolated from mangosteen pericarp.

Materials and Methods

Chemicals and reagent

α-Mangostin from the fruit rind of *G. mangostana* was purchased from Indofine (NJ, USA). Scopolamine HCl, *N*-Acetyl-Asp-Glu-Val-Asp *p*-nitroanilide (Ac-DEVD-*p*NA), acetylcholinesterase (Type VI-S) from *Electrophorus electricus* (electric eel), ABTS, acetylthiocholine iodide (ATChI), ascorbic acid (AA), β-naphthyl acetate (NA), butylated hydroxytoluene (BHT), donepezil (DPZ), DPPH, 5,5'-dithiobis(2-nitrobenzoate) (DTNB), dithiothreitol (DTT), ethylenediaminetetraacetic acid (EDTA), fast blue B (FB) salt, ferric chloride, hydrochloric acid (HCl), methanol, potassium *ferricyanide*, quercetin (QCT), sodium chloride (NaCl), thiobarbituric acid (TBA), trichloroacetic acid (TCA), and tris(hydroxymethyl)aminomethane hydrochloride (Tris-HCl), and Triton-X 100 were all purchased from Sigma-Aldrich (St. Louis, MO, USA).

Ferric reducing antioxidant power in vitro

Several concentrations of α-MG were examined for the FRAP using the assay explained [17], with minor modifications. Various concentrations of α-MG, DPZ, or standard (ascorbic acid, AA) solutions (1 mL) were mixed with 2.5 mL of 1% (w/v) potassium ferricyanide $K_3[Fe(CN)_6]$ and 2.5 mL of 0.1 M potassium phosphate buffer (pH 7.4). The solution was added to 2.5 mL of 10% TCA after boiling for 20 min at 50°C. All the ingredients were centrifuged at a speed of 3,300 g for 10 min. After that, 2.5 mL of the supernatant was added to 0.5 mL of 0.1% (v/v) ferric chloride ($FeCl_3$) and mixed with 2.5 ml Lof distilled water. The optical density of the mixture was measured at 593 nm.

$ABTS^{\bullet+}$ radical scavenging assay in vitro

The ABTS radical cation assay was firstly described for the determination of antioxidant activity [18]. Various concentrations of α-MG were examined for ABTS radical scavenging capacity following the previously described assay with minor modifications [19-20]. Firstly, $ABTS^{\bullet+}$ was generated by reacting $ABTS^{\bullet+}$ stock solutions (7 mM) with potassium persulfate (2.45 mM) in distilled water and the resultant solution was left in the dark place for 16 h. Fifty μL of α-MG, DPZ, or QCT at various concentrations was mixed with 2.5 mL of ABTS in 0.1 M phosphate buffer (pH 7.4) with an optical density (OD) of 0.75 ± 0.02 at 420 nm, which produced percentage inhibition of the blank OD between 20-80. The solution was left at 30°C for 10 min and OD at 420 nm was measured. The percentage of $ABTS^{\bullet+}$ radical scavenging activity was calculated and expressed as IC_{50} values.

DPPH radical scavenging assay in vitro

DPPH method of the antioxidant assay was performed as described [21]. Different concentrations of α-MG were examined for DPPH radical scavenging activity following the assay explained with minor modifications [22]. Firstly, 0.5 mL solution of α-MG, DPZ, or standard (butylated hydroxytoluene, BHT) solution at various concentrations was added into 3 mL of 0.5 mM DPPH radical in methanol solution and left at 25°C for 45 min until the reaction was finished in the dark place. The OD of the mixture was measured at 519 nm.

AChE inhibitory activity by Ellman assay in vitro

The assay of acetylcholinesterase (AChE) inhibition was measured following the Ellman's colorimetric method previously described with minor modifications [23-25]. Thiocholine, produced from the hydrolysis of acetylcholine iodide (ATChI) by AChE, reacts with Ellman's reagent (5,5′-dithiobis-2-nitrobenzoic acid or DTNB) to give 5-thio-2-nitrobenzoic acid (TNB) with a yellow color, which is proportional to the AChE activity present. The procedure was as follows: firstly, 25 μL of α-MG, DPZ, or standard eserine (ESR) in 0.1 M phosphate buffer (pH 7.4) was added into 25 μL of 0.22 U/mL AChE enzyme solution and left for 15 min at 37°C. After mixing with Ellman's solution [25 μL of 1.5 mM ATChI, 125 μL of 3 mM DTNB, and 25 μL of 0.1 M phosphate buffer (pH 7.4)], the optical density at 405 nm was measured promptly. The optical density was measured every 2 min for 10 min to calculate the reaction velocities.

Before being expressed as IC_{50} values, the percentage of AChE inhibitory activity was calculated using the following equation:

Inhibition (%) = 1 – (Asample/Acontrol) × 100

AChE inhibitory activity by NA-FB assay in vitro

The AChE inhibitory activity was performed using the β-naphthyl acetate-fast blue B (NA-FB) assay previously explained with minor modifications [26]. Firstly, 10 µL of α-MG, DPZ, or standard ESR in 0.1 M phosphate buffer (pH 7.4) was mixed with 200 µL of 3.33 U/mL AChE enzyme solution and left at 37°C for 15 min. The mixture was added with 50 µL of 0.25 mg/mL NA, dissolved in methanol, and left at 4°C for 40 min. Measure optical density at 600 nm immediately after mixing with 10 µL of 2.5 mg/mL FB dissolves in water to mix with the above reaction. The percentage of inhibition for each test solution was calculated as mentioned above.

Animals designing and treatment

The Animal Care and Use Committee of Suranaree University of Technology approved all animal experimental procedures. Sixty-four 8-week-old male Wistar rats (250±50 g) were provided by the Laboratory Animal Center of Suranaree University of Technology. Animals were maintained on 12-h light-dark cycle in a temperature-controlled (20±1°C) chamber and allowed food and water *ad libitum*. All animal experiments were carried out strictly according to the Guide for the Care and Use of Laboratory Animals of Suranaree University of Technology (No. 9/2557). Animals were randomly divided into 8 groups: 2 groups of vehicle (treated with 2% Tween80 as vehicle control), 2 groups of DPZ (treated with donepezil 2 mg/kg), 2 groups of α-MG50 (treated with α-MG 50 mg/kg), and 2 groups of α-MG100 (treated with α-MG 100 mg/kg). All drugs were intraperitoneally administered for 7 days. Sixty minutes after daily administration of all drugs, animals from each treatment were intraperitoneally administered with normal saline solution or 2 mg/kg of scopolamine HCl to generate a SCOP model. Rats were weighed before and after treatment.

Collection of blood and brain samples

The rats in each group were anesthetized at the end of the experimental period using Nembutal sodium (60 mg/kg, i.p.) and blood was obtained through the puncture of the left ventricle into heparinized tubes. Heparinized blood was centrifuged at 2,000 g for 5 minutes, obtained plasma was stored at -20 °C until further biochemical analysis. After blood collection, the rats were perfused with ice-cold normal saline solution (0.9% NaCl) and decapitated. The brains were rapidly removed and placed on a petri dish filled with ice. The cerebral cortex, hippocampus, and basal forebrain were dissected after localization according to the rat brain in stereotaxic coordinates [27]. The dissected brain structures were weighed and homogenized in ice-cold PBS to obtain 10% tissue homogenate followed by centrifugation at the speed of 10,000 g for 15 min at 4°C. The supernatant was collected for the assay of lipid peroxidation and caspase-3 activity.

Determination of plasma biochemical parameters

The plasma biochemical parameters [aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH)] were investigated by A15 Automatic Clinical Chemistry (BioSysyems S.A., Spain).

Determination of lipid peroxidation inhibition activity

Determination of lipid peroxidation inhibitory activity was performed as described [28]. Briefly, 100 µL of the samples of brain homogenate were incubated with either 100 µL TBARS (thiobarbituric acid reactive substance) solution including 15% (w/v) TCA, 0.375%TBA, and 0.25 N HCl, was mixed thoroughly, or 100 µL TBARS solution containing the above together with 0.02% w/v BHT, was added. Samples were then mixed vigorously and heated for 15 min at 95°C. After cooling, followed by centrifugation at 3,000 g for 10 min at 4°C. The absorbance of the solution was measured at 532 nm using the extinction coefficient of 1.56×10^5 L/mal.cm. The results were compared with their control and they were expressed as µmol/g of brain tissue protein.

Determination of caspase-3 activity

Caspase-3 activity assay was performed using a colorimetric method [29]. Briefly, the rat brain homogenates were washed in caspase-3 lysis buffer containing 10 mM Tris-HCl, pH 7.4, 0.5M NaCl, 1 mM EDTA, 5 mM DTT, and 0.1% Triton-X 100. The brain homogenates were incubated on ice for 15 min and centrifuged at 15,000 g for 15 min at 4°C. The protein concentration was determined by the Lowry method and the caspase-3 activity in the supernatant was measured immediately. 50 g protein samples in 10 µL were added to 980 µL assay buffer. The reaction was initiated by adding 10 µL of 20 mM of the caspase-3 substrate Ac-DEVD-*p*NA. The tubes were covered and incubated at 37°C overnight. Cleavage of the chromophore from the substrate was detected spectrophotometrically at a wavelength of 405 nm.

Statistical analysis

Data were calculated as mean ± SEM. To compare between treatment groups, this collected info was analyzed by using one-way ANOVA and the *Student's t-test* followed by *post-hoc* Newman-Keuls (SigmaStat

version 3.5). The statistically significant levels were considered at P values of < 0.05. All graphical analyses were accomplished using GraphPad Prism version 6.0 (GraphPad®, CA, USA).

Results

α-MG reduces ferric iron (Fe^{3+}) to ferrous iron (Fe^{2+})

Based on the results obtained, figure 1A shows ferric reducing antioxidant power of α-MG, DPZ, and AA, reference standard. All test compounds revealed dramatically reducing power: 100-600 mg/mL α-MG, DPZ, and AA provided absorbance within the range of 20-410 µmol Fe^{2+}/L. All compounds significantly increase the optical density, indicating the antioxidant potential of α-MG. The FRAP value of the reference standard and the compounds were in the order of AA, α-MG, and DPZ, respectively.

α-MG scavenges $ABTS^{\bullet+}$ radicals

The results of the $ABTS^{\bullet+}$ radical scavenging method are shown in figure 1B, which revealed the free radical scavenging activity of ABTS of α-MG, DPZ, and QCT, reference standard. A significant reduction in ABTS free radical concentration occurred during the scavenging process. The percentage of ABTS scavenging at different concentrations showed that α-MG has the ability to eliminate free radicals with the half-maximal inhibitory concentration (IC_{50}) at 21.52 ± 3.45 µg/mL, which is similar to the standard quercetin (IC_{50} = 28.01 ± 2.15 µg/mL). DPZ also demonstrated potent radical scavenging property with IC_{50} at 14.53 ± 1.86 µg/mL.

α-MG scavenges DPPH radicals

Based on the results obtained, figure 1C shows the DPPH radical scavenging activity of α-MG, DPZ, and BHT, reference standards. The percentage inhibition of DPPH free radicals at different concentrations showed that α-MG has a potential anti-radical activity with an IC_{50} of 38.12±8.36 µg/mL, which is similar to BHT (IC_{50} = 42.21±6.73 µg/mL), the reference standard. DPZ also revealed strong radical scavenging activity with IC_{50} values of 29.44±5.13 µg/mL.

α-MG inhibits AChE activity

The AChE inhibitory activity of α-MG purified from *G. mangostana* with eel AChE was examined by Ellman's or NA-FB methods using ATChI-DTNB (Figure 2A) or NA-FB (Figure 2B), respectively. The AChE activity is evaluated when thiocholine reacts with DTNB ion or when β-naphthol reacts with FB. The results of current studies showed that α-MG purified from *G. mangostana* inhibited eel AChE in a dose-dependent manner (Figure 2). Maximal activity (75%) was discovered in α-MG and more than the ac-

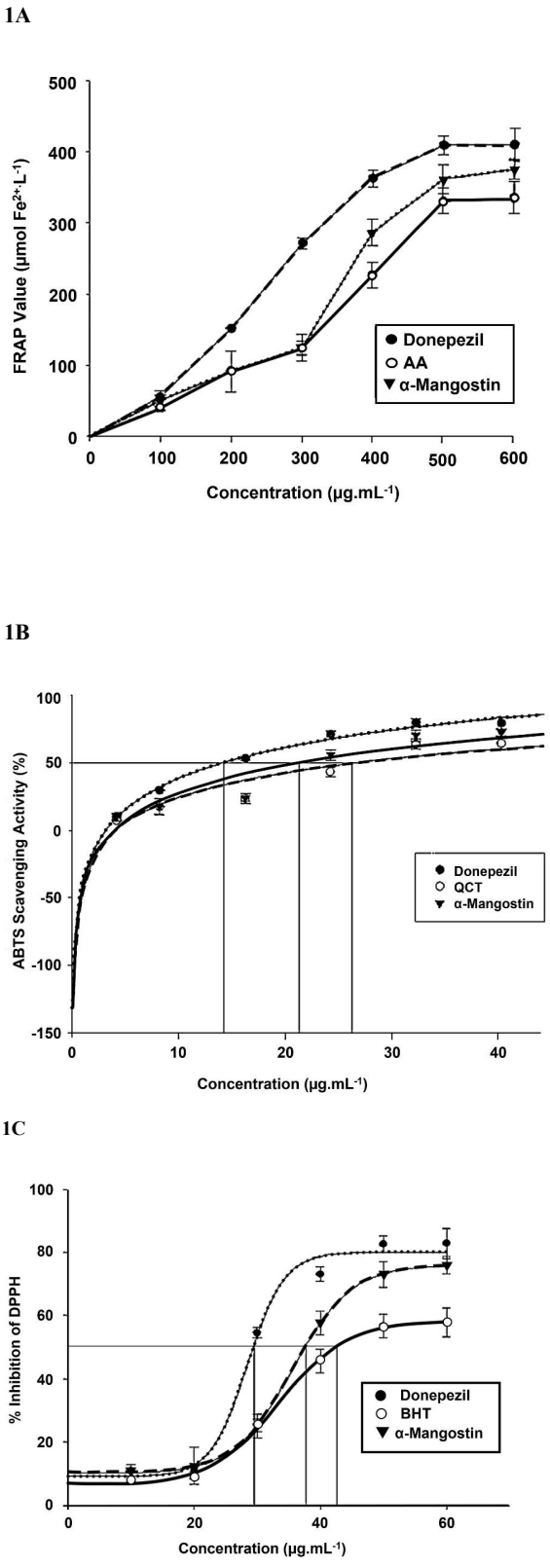

Figure 1. Effects of α-MG purified from the fruit rind of *G. mangostana*, DPZ, and the reference standard on 1A; FRAP *in vitro*. FRAP; ferric reducing antioxidant power, 1B; $ABTS^{\bullet+}$ radical scavenging activity; 1C; DPPH radical scavenging activity.

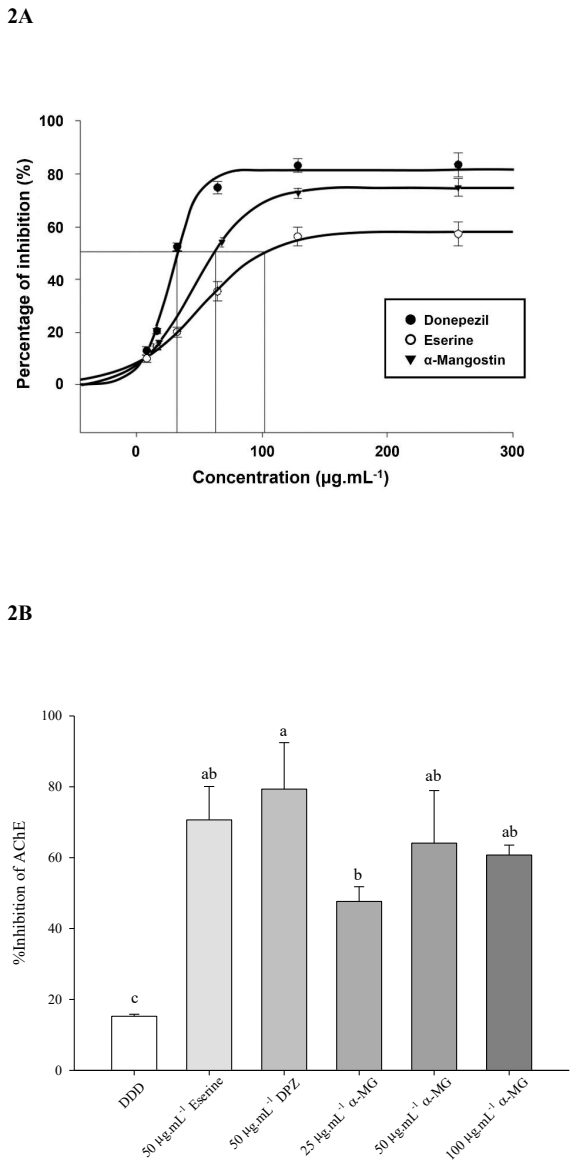

Figure 2. Effects of α-MG purified from the fruit rind of *G. mangostana*, DPZ, and reference standard eserine on acetylcholinesterase inhibitory activity *in vitro* measured by 2A; Ellman's method, 2B; NA-FB method. Each value is expressed as mean ± SD. Different alphabets indicate significantly different ($p<0.05$), compared with their control group.

tivity of the ESR (55%) under the same conditions. DPZ, a potential anti-AChE inhibitor, reduced AChE activity by 80%.

α-MG does not significantly change plasma biochemical parameters and body weight

The results showed plasma biochemical parameters [creatinine, AST, ALT, and LDH] of SCOP-induced amnesic rats intraperitoneally administration with the α-MG purified from the fruit rind of *G. mangostana* and DNP for 7 consecutive days. In all instances, administration of all doses of α-MG revealed no effect on the food and water intake and behavior of the rats. After 7-day administration of all doses of α-MG, their body weight changes (Figure 3) and LDH plasma level did not alter from those of the vehicle control. In NSS groups, plasma AST levels were decreased after administration of donepezil and the α-MG (100 mg/kg) as shown in figure 4A. Scopolamine significantly increased plasma ALT levels. In SCOP groups, plasma

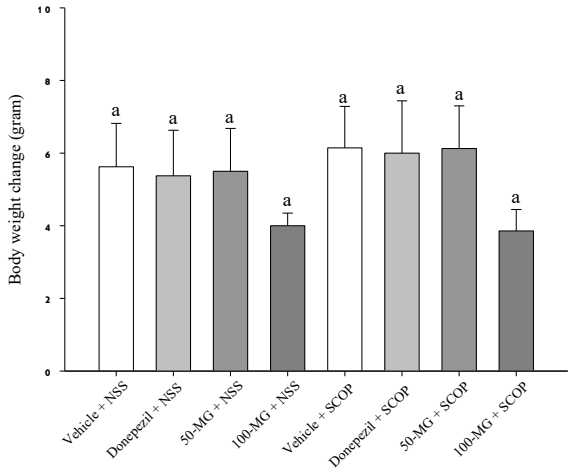

Figure 3. Effect of α-mangostin purified from *G. mangostana* and donepezil on the percentage of body weight changes in normal saline-treated rats and scopolamine-induced amnesic rats. Values are expressed as means ± S.E.M; n = 8 per group. Different alphabets indicate significant difference, $P<0.05$.

ALT level was decreased after administration of the α-MG (100 mg/kg) as shown in figure 4B.

α-MG ameliorates lipid peroxidation

The percentage of lipid peroxidation inhibition indicated that α-MG at a dose of 50 mg/kg possessed the highest potential inhibitory activity. In NSS treatment, the results were not significantly different between groups in all studied brain regions. SCOP significantly elevated MDA levels in all regions of the brain, compared with the respective NSS groups ($P<0.05$) as shown in figure 5A, 5B, and 5C. Pretreatment with DPZ and α-MG (50 mg/kg) significantly attenuated the increase of MDA level in the cerebral cortex and hippocampus ($P<0.05$) induced by SCOP, but not α-MG (100 mg/kg), as shown in figure 5A and 5B. None of the pretreatments could affect MDA level in the basal forebrain induced by SCOP.

α-MG inhibits caspase-3 activity

The results showed that no significant difference was found between groups in NSS treatment in all studied brain regions. SCOP significantly elevated caspase-3 activity in all brain regions, compared to their respective NSS groups ($P<0.05$) as shown in Fig. 6A, 6B, and 6C. Pretreatment with DPZ and α-MG (50 mg/kg),

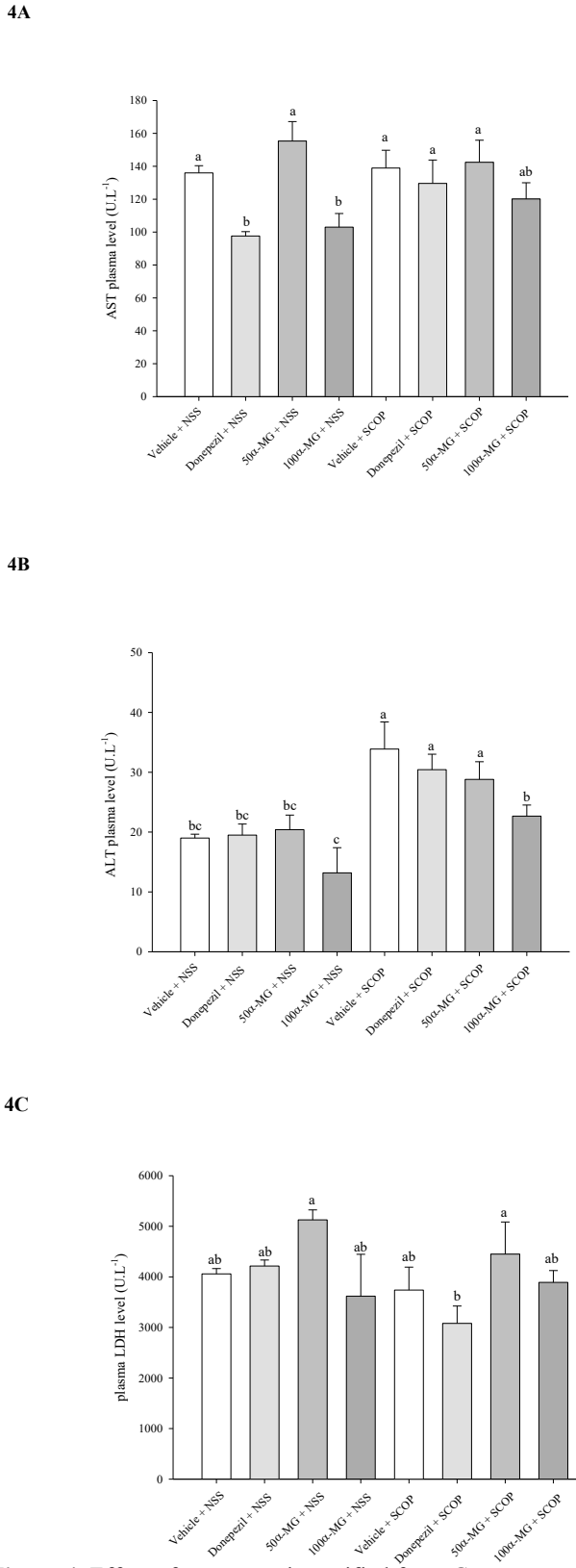

Figure 4. Effect of α-mangostin purified from *G. mangostana* and donepezil on plasma biochemical parameters in 4A; AST, 4B; ALT, 4C; LDH of normal saline-treated rats and scopolamine-induced amnesic rats. Values are expressed as means ± S.E.M; n = 8 per group. Different alphabets indicate significant differences, P<0.05.

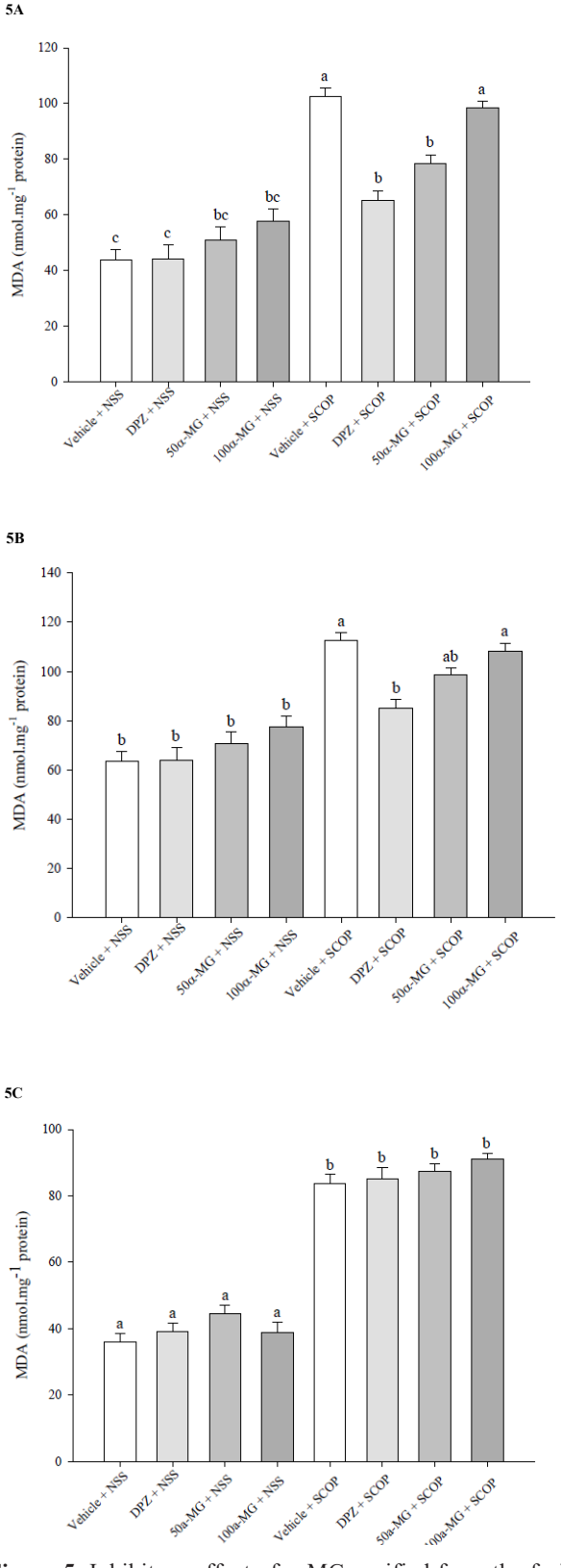

Figure 5. Inhibitory effect of α-MG purified from the fruit rind of *G. mangostana* and DPZ on LPO in 5A; cerebral cortex, 5B; hippocampus, 5C; basal forebrain of NSS-treated rats and SCOP-induced amnesic rats. Each value is expressed as mean ± SEM.* p<0.05, compared with the control group; ** p<0.05, versus SCOP only treated group.

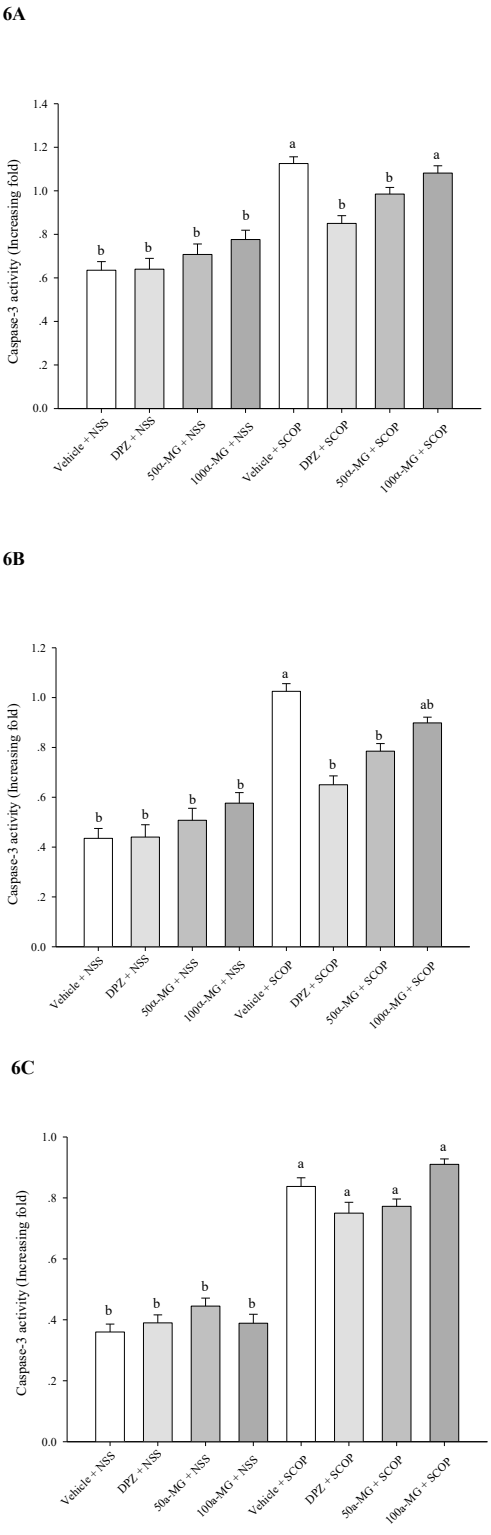

Figure 6. Effects of the α-mangostin purified from the fruit rind of *G. mangostana* and donepezil on catalytic activity of the caspase-3 enzyme in the 6A; cerebral cortex, 6B; hippocampus, 6C; basal forebrain of normal saline-treated rats and scopolamine-induced amnesic rats. Values are expressed as means ± S.E.M; n = 8 per group and are the average of three independent. Different alphabets indicate significant difference, P<0.05.

but not α-MG (100 mg/kg), significantly attenuated the elevation of caspase-3 activity induced by SCOP in the cerebral cortex and hippocampus (P<0.05) as shown in Figure 6A and 6B. In the basal forebrain, none of the pretreatments could affect the increase of caspase-3 activity induced by SCOP (Figure 6C).

Table 1. Half maximal inhibitory concentrations (IC_{50}) for several assays of α-MG

Assays	Half maximal inhibition (IC_{50})	
	α-MG	DPZ
ABTS (μg/mL)	21.52±3.45[a]	14.53±1.86
DPPH (μg/mL)	38.12±8.36[a]	29.44±5.13
AChE (mg/mL)	64.23±0.22[a]	32.46±0.14

Each value is expressed as mean ± SEM. (p<0.05)
[a] indicate that significant difference when compared with their DPZ control groups

Discussion

Alpha-MG has been revealed to show ROS scavenging activity [15]. FRAP is an important indicator of the potential antioxidant activity due to the ability of free radicals to decompose *via* donating hydrogen atoms. FRAP assay is a direct measurement of the total antioxidant activity of biological substances [30]. Ferric reducing ability of α-MG at various concentrations was verified by methods previously reported [17], which are dependent on the redox reaction of ferric (Fe^{3+}) cyanide complexes to ferrous (Fe^{2+}) by donating electrons. Extensive evidence suggests that ROS, which builds up in the midst of oxidative stress, causes abnormalities of cells and molecules [31-33]. ABTS antioxidant assay is based on the capacity of ABTS, antioxidant compounds reduce the free radicals and get themselves oxidized. DPPH is a very stable free radical and reacts with compounds that can detect the number of changes in optical density by expressing the percentage of scavenging activity. Reduction by antioxidant compounds results in the color change of the reagent, which correlates with the antioxidant capacity, which is measured by the change in absorbance. ROS has a significant contribution in nerve damage in AD [34]. Free radical scavenging activity is absolutely necessary to prevent the harmful effects of free radicals in AD. The compounds, either plant or plant-derived molecules, that modulate cholinesterase activity and multiple components of the oxidative stress pathway would be effective candidates for potential drugs that restrict the development of AD [35]. Many phytochemicals are extracted from plants, which help diminish oxidative stress, inhibit apoptosis and reduce the activity of AChE [36-37]. Antioxidant, antiapoptosis and AChE inhibitory properties of α-MG were explained by its core structure xanthone. Xanthone is one of the most potent antioxidants in the plant king-

dom and has been confirmed to have chemopreventive effects [38]. The antioxidant activity of organic compounds such as xanthone, especially from *G. mangostana*, is believed to be the result of redox abilities [39]. We previously found that the crude extract of *G. mangostana* also possesses AChE inhibitory properties and antioxidant activities, and does not affect the levels of AST and ALT [14]. The present results agree with the previous report that both AST and ALT are enzymes produced by liver cells that were released when liver cells were damaged [40]. The possible mechanism of the effect of α-MG on the reduction of ALT levels may be related to a reduction in levels of plasma free fatty acid (FFA), a reduction in FFA flux into the liver, and an increase in hepatic insulin sensitivity [41]. No toxicological signs were found in any of the plasma biochemical parameters and body weight changes between all treatment groups. Intraperitoneal administration of the α-MG purified from the fruit rind of *G. mangostana* and DPZ did not affect the behavior of SCOP-induced amnesic rats.

MDA is a product of lipid peroxidation and has been used as a well-established biomarker of oxidative stress [42]. The results of lipid peroxidation revealed the increase of MDA, induced by scopolamine, was normalized by α-MG purified from *G. mangostana* in the cerebral cortex and hippocampus. The previous study showed the inhibition of lipid oxidation by α-MG and reduced oxidative damage in rat brain tissue [43-44]. The present results indicated that α-MG could act as an inhibitor of lipid peroxidation of the rat cerebral cortex and hippocampus. Similar to the *S. minor* extracts, α-MG purified from *G. mangostana* attenuated both AChE activity and oxidative injury in the brain as evidenced by the decreased malondialdehyde level [45]. The apoptotic process has an important role in the neurodegeneration of Alzheimer's disease [46]. The results of apoptosis revealed the increase of caspase-3 activity by scopolamine; while α-MG purified from *G. mangostana* inhibited apoptosis in the cerebral cortex and hippocampus. Alpha-MG has been previously revealed to show antiapoptotic and neuroprotective effects and acted against $CoCl_2$-induced apoptosis by suppressing oxidative stress [16,47]. The present results indicated that α-MG could act as an inhibitor of apoptosis of the rat cerebral cortex and hippocampus.

Conclusion

Our study found that α-MG purified from *G. mangostana* demonstrated a neuroprotective effect against SCOP neurotoxicity. Also, the present study is the first report about α-MG, a potential neuroprotective candidate, which facilitate brain function by ameliorating scopolamine-induced neurotoxicity through inhibition of lipid peroxidation and caspase-3 enzyme activity in the cerebral cortex and hippocampus.

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Conflict of Interests

The authors report no conflicts of interest.

Acknowledgment

None.

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