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Research Article

Jasonia Montana; A Promising Therapeutic Agent to Attenuate Neurological Disorders Associated with SCO-induced Dementia

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Abstract

Neurodegenerative disorder clinically characterized by progressive cognitive and memory dysfunction. This study investigated the effect of Jasonia montana ethanolic extract (JMEE) on Ca-, Mg^{+2} and Na^{+}, K^{+}-ATPase and acetylcholinesterase (AChE) activities as well as β amyloid1-42 level in brain hippocampus of adult rats exposed to SCO. Rats were exposed to SCO (3.0 mg/Kg) and JMEE (150 mg/Kg) by gavage for 14 days. Rats were randomly divided into six groups with 6 rats in each: [Saline], [saline/SCO (3.0 mg/kg)], [saline/SCO (3.0 mg/kg)/JMEE (150 mg/kg,)], [saline/SCO (3.0 mg/kg)/ DHC (3 mg/kg)] and [saline/SCO (3.0 mg/kg)/JMEE (150 mg/kg,)/ DHC (3 mg/kg)]. Results demonstrated that plasma TC, TG as well as brain hippocampus levels of AChE, MAO, βA1-42, TBARS. Also, the results showed that a significant depletion of plasma HDL-C as well as brain hippocampus levels of phospholipids, GSH, ACh, Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase. Treatment with JMEE (150 mg/Kg) prevented the increase in TC, TG, AChE, MAO, β amyloid1-42, TBARS activity when compared to SCO-treated group. JMEE treatment prevented the SCO-induced decrease in Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activities as well as GSH, HDL-C, ACh and phospholipids in SCO-treated group when compared to normal group. Our data showed that JMEE have a protector effect against SCO induced neurodegenerative. Also, Jasonia Montana is a promising therapeutic agent to attenuate neurological disorders associated with SCO induced dementia.

Keywords: Jasonia Montana; Antioxidant; Scopolamine; Acetylcholine Esterase; Monoamine Oxidase and Dementia

Abbreviations

JMEE: Jasonia Montana Ethanolic Extract; DHC: Donepezil Hydrochloride; AChE: Acetylcholinesterase; SCO: Scopolamine; TC: Total Cholesterol; TG: Triglycerides; MAO: Monoamine Oxidase; βA1-42: β amyloid1-42; TBARS: Thiobarbaturic Acid Reactive Substances; HDL-C: Cholesterol-High Density Lipoprotein; GHS: Reduced Glutathione.

Introduction

Neurodegenerative diseases are an incurable group of degenerative disorders. They are characterized by loss of neuronal cells, leading to progressive impairments of functions of central nervous system (CNS) [1]. Neurons are affected when a genetic mutation is identified in a ubiquitously expressed gene. For examples, the mutations in amyloid precursor protein (APP) or presenilin 1 (PSEN1) and 2 (PSEN2) that occur in Alzheimer's disease (AD) [1], which affect learning and memory circuits [2,3].

However, during aging and various disease states, antioxidant defense systems can be altered leading to progressive oxidative damage and subsequent cell death and/or significant loss of function [4,5]. The brain is particularly sensitive to oxidative stress since it presents: high content of peroxidizable unsaturated fatty acids, high oxygen consumption per unit of weight, high content in iron and ascorbate (LPO key ingredients) and a scarcity of antioxidant defense systems (e.g. GSH, GPx, CAT and vitamin E) [6-11]. In humans, the brain accounts for only a few percent of the body weight, but it processes 20 % of basal oxygen consumption. A neuron uses much of oxygen via mitochondrial respiratory chain to make ATP for maintaining low gradients [12,13].

Plant-derived polyphenols have been implicated as beneficial agents in a multitude of disease states [14,15], most commonly cancer, cardiovascular disease, and neurodegenerative disorders. Flavonoids are also able to counteract the neuronal injury underlying these disorders and thus slowing the disease progression [16,17]. They have been shown to be effective at blocking oxidant-induced neuronal injury [18], although not via direct radical or oxidant-scavenging activity [19,20].

Jasonia Montana occurs in the Mediterranean and adjacent areas [21], including the *Sinai Peninsula* [22]. The herb has a strong aromatic odor and is used in traditional medicine for diarrhea, stomachache, and chest diseases [23].

Polyphenols [24], mono- and sesquiterpenes [25], flavonoids [26], and essential oils [27] have been reported from Jasonia Montana represent a promising potential species [28]. These polyphenols are more potent antioxidants than vitamins C and E [29]. Also, of the aerial parts of J. Montana was reported. In-vivo tests have been conducted with Jasonia Montana to determine, for example, its antioxidant [30], hypoglycemic [31], anticholestatic [32] and anti-obesity [33] activities. But there are no reports of the neuroprotective effect of Jasonia Monta. The present study was undertaken to investigate the investigated the effect of Jasonia Montana extract antioxidant activity against scopolamine induced neurotoxicity.

Materials and Methods

Chemicals

Scopolamine hydrobromide and donepezil hydrochloride was obtained from Sigma Chemical Co. (St. Louis MO, USA).

Plant material

Fresh aerial parts of J. Montana were collected from the Sinai Peninsula the plant was identified by Prof. Heba A. Elgizawy, Pharmacognosy department, Faculty of Pharmacy, October 6 University.

Preparation of ethanolic extract

Air-dried aerial parts of the plant (1.5 kg) was crushed to coarse powder and extracted exhaustively in a Soxhlet with 95% ethanol. The extract was concentrated under reduced pressure to yield viscous mass. The ethanolic extract was kept in airtight containers in a deep freeze maintained at 4°C until the time of further use.

Phytochemical screening

A phytochemical analysis of aerial parts of J. Montana was conducted for the detection of alkaloids, cardiac glycosides, flavonoids, tannins, anthraquinones, saponins, volatile oil, coumarins and triterpenes [34].

Animals

Adult albino rats weighing around 150 ± 10 gms, at the age of 10 weeks were purchased from National Cancer Institute, Cairo University. They were acclimatized to animal house conditions. Animals were provided with standard diet and water ad libtum. Rats were kept under constant environmental condition and observed daily throughout the experimental work.

Experimental design

The rats were randomized and divided into five groups of six rats each. Food was withdrawn 24 h and water 2 h before the commencement of experiment. The animals were divided into the following groups (Table 1).

No.	Groups	Treatment Description
I	Normal control	Received 5 mL saline orally, daily for 14 days.
II	Disease control	Received Scopolamine hydrobromide (SCO) (3 mg/kg.b.w. i.p), daily for 14 days [35].
III	Treated group (A)	Received SCO (3 mg/kg.b.w. i.p.) + J. Montana ethanolic extract (150 mg/kg b.w. orally) daily for 14 days [32].
IV	Treated group (B)	Received SCO (3 mg/kg.b.w.i.p.) + donepezil hydrochloride (3 mg/kg, orally) daily for 14 days [36].
V	Treated group (C)	Received SCO (3 mg/kg.b.w. i.p.) + J. Montana ethanolic extract (150 mg/kg b.w. orally) + donepezil hydrochloride (3 mg/kg, orally).

Table 1: Groups of animals in the present study.

Plasma lipid profile estimation

On 15th day, blood was collected from the retro-orbital vein of each animal and each sample was collected into heparinized tubes, centrifuged, and plasma was used freshly for estimation of plasma plasma triglyceride, total cholesterol and HDL- cholesterol were determined using commercially available kits (Asan and Young-dong Pharmaceutical Co., Korea) [37-39], respectively.

Preparation of brain samples

Rats were dissected by cervical dislocation, and then brain hippocampus were rapidly removed, extracted with saline at the mass-liquid ratio of 1:9, then the tissue homogenate was centrifuged at 3500 r/min for 10 min. The homogenate was divided into five aliquots. The first one was deproteinized with ice-cooled 12% trichloroacetic acid and the obtained supernatant, after centrifugation at 1000 xg, was used for the estimation of GSH level. The second aliquot was centrifuged at 1000 xg and the resultant supernatant was used for estimation of acetylcholine esterase (AChE) and monoamine oxidase (MAO) activity as well as thiobarbaturic acid reactive substances (TBARS), acetylcholine (ACh) and total protein content s using immunoassay kits (Immuno-Biological Laboratories ELISA kit). The third aliquot of brain homogenate was centrifugated at 10500 xg for 15 min at 4 °C using a cooling ultra-centrifuge (Sorvall comiplus T-880, Du Pont, USA), and the clear supernatant was used for the determination of Ca^{+2}, Mg^{+2}, Na^{+}, K^{+}-ATPase activities. The fourth aliquot used to extract and separate phospholipids according to Tokeo and Sakanashi method [40]. Briefly, 1 mg of homogenized tissue was treated with 950 µL of chloroform: methanol (2:1, v: v) solution containing butylated hydroxytoluene (2 mM) and 50 µL of potassium phosphate buffer (100 mM, pH 7.4). The fifth aliquot was centrifuged at 5000 xg, and the supernatant was used for the detection of β – Amyloid (Aβ1-42). Standard curve analysis was run in parallel to test samples. The absorbance was measured in the multi-scan spectrum spectrophotometer (Thermo Scientific, Multiskan GO) at optical density 450 nm. All the readings were performed in triplicate.

Histological assessment

The brain hippocampus was sliced, and pieces were fixed in 10% buffered formaldehyde solution for histological study. The fixed tissues were processed by automated tissue processing machine. Tissues were embedded in paraffin wax by conventional methods. Sections of 5 lm in thickness were prepared and then stained with hematoxylin and eosin for light microscopy analyses according to the method of Bancroft and Steven [41]. After that, the sections were observed under the microscope for histopathological changes, and their photomicrographs were captured.

Statistical analysis

The results were expressed as means ± SD. Comparisons between groups were performed using one-way analysis of variance (ANOVA). Differences between individual treatment groups were compared using Dunnett's test. Statistical significance was set at $P < 0.05$ and $P < 0.01$, and the statistical analyses were performed using SPSS software, version 15.0 (SPSS, Inc., Chicago, IL, USA).

Results

Table 2 showed that oral administration of scopolamine hydrobromide (3 mg/kg.b.w. i.p) resulted in a significant increase in plasma cholesterol and triglycerides as well as significantly decreased of plasma high-density lipoprotein-cholesterol (HDL-C) and brain hippocampus phospholipids when compared to the normal control group ($p < 0.01$). Supplementation of J. Montana ethanolic extract (150 mg/kg b.w.) and donepezil hydrochloride (3 mg/kg, orally)

individually or in combination resulted in a significant decrease in plasma cholesterol and triglycerides as well as significant increased plasma HDL-C and brain hippocampus phospholipids compared to the group that received scopolamine hydrobromide ($p < 0.05$). The effect of combination more pronounced than their administration individuality.

Groups	Treatment Description	Cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	Phospholipids (mg/g tissue)
I	Normal control (5 mL saline)	78.55 ± 2.88[a]	64.98 ± 4.23[a]	34.87 ± 4.00[d]	956.65 ± 12.66[e]
II	Scopolamine hydrobromide (SCO) (3 mg/kg.b.w.)	132.98 ± 7.37[e]	184.55 ± 9.48[d]	21.54 ± 4.66[a]	474.55 ± 18.70[a]
III	SCO (3 mg/kg.b.w. i.p.) + J. montana ethanolic extract (150 mg/kg b.w.)	96.06 ± 4.32[d]	84.15 ± 5.85[c]	30.76 ± 3.65[c]	838.09 ± 16.48[c]
IV	SCO (3 mg/kg.b.w.i.p.) + donepezil hydrochloride (3 mg/kg.)	110.56 ± 8.48[c]	85.44 ± 6.73[c]	25.40 ± 4.48[b]	766.84 ± 11.47[b]
V	SCO (3 mg/kg.b.w.) + J. montana ethanolic extract (150 mg/kg b.w.) + donepezil hydrochloride (3 mg/kg.).	84.66 ± 4.98[b]	73.11 ± 5.43[b]	33.25 ± 2.98[d]	879.55 ± 18.70[d]

Table 2: Levels of plasma cholesterol, triglycerides and cholesterol-high density lipoprotein (HDL) as well as brain hippocampus phospholipids in normal and experimental groups of mice.

Values represent the mean ± SE (n = 6). Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at $P \leq 0.05$.

Table 3 showed that oral administration of scopolamine hydrobromide (3 mg/kg.b.w. i.p) resulted in a significant increase in brain hippocampus lipid TBARS and monoamine oxidase (MAO) compared to the normal control group ($p < 0.01$). Supplementation of J. Montana ethanolic extract (150 mg/kg b.w.) and donepezil hydrochloride (3 mg/kg, orally) individually or in combination resulted in a significant decrease in brain hippocampus lipid TBARS and monoamine oxidase (MAO) compared to the group that received scopolamine hydrobromide (3 mg/kg.b.w. i.p) ($p < 0.05$). Also, oral administration of scopolamine hydrobromide (3 mg/kg.b.w. i.p) resulted in a significant decrease in brain hippocampus cetylcholine (ACh), reduced glutathione (GSH) contents as well as acetylcholine esterase (AChE) activity, compared to the normal control group ($p < 0.01$). Supplementation of J. Montana ethanolic extract (150 mg/kg b.w.) and donepezil hydrochloride (3 mg/kg, orally) individually or in combination resulted in a significant increase in GSH, Ach, and AChE compared to the group that received scopolamine hydrobromide (3 mg/kg.b.w. i.p) ($p < 0.05$). The effect of combination formula more pronounced than their administration individuality.

Table 4 showed that oral administration of scopolamine hydrobromide (3 mg/kg.b.w. i.p) resulted in a significant increase in brain hippocampus β amyloid1-42 as well as significantly decreased of brain hippocampus Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activity when compared to the normal control group ($p < 0.01$). Supplementation of J. Montana ethanolic extract (150 mg/kg b.w.) and donepezil hydrochloride (3 mg/kg, orally) individually or in combination resulted in a significant decrease in brain hippocampus β amyloid1-42 as well as significantly increased of brain hippocampus Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activity when compared to the group that received scopolamine hydrobromide (3 mg/kg.b.w. i.p) ($p < 0.05$). The effect of combination more pronounced than their administration individuality.

Groups	Treatment Description	TBARS (nmole MDA/ mg protein)	GSH (µM/mg protein)	ACh (mM/mg protein)	Ach E (U/mg protein)	MAO (U/mg protein)
I	Normal control (5 mL saline)	15.48 ± 1.22[a]	0.52 ± 0.031[d]	8.54 ± 0.54[c]	0.45 ± 0.05[a]	23.87 ± 2.15[a]
II	Scopolamine hydrobromide (SCO) (3 mg/kg.b.w.)	32.45 ± 3.66[d]	0.15 ± 0.025[a]	4.33 ± 0.65[a]	1.43 ± 0.13[e]	43.76 ± 4.56[d]
III	SCO (3 mg/kg.b.w. i.p.) + J. montana ethanolic extract (150 mg/kg b.w.)	18.66 ± 2.04[b]	0.43 ± 0.05[c]	7.54 ± 0.47[b]	0.85 ± 0.08[d]	25.90 ± 3.76[ab]
IV	SCO (3 mg/kg.b.w.i.p.) + donepezil hydrochloride (3 mg/kg)	22.15 ± 2.71[c]	0.39 ± 0.04[b]	7.10 ± 0.54[b]	0.94 ± 0.05[c]	29.48 ± 2.87[c]
V	SCO (3 mg/kg.b.w.) + J. montana ethanolic extract (150 mg/kg b.w.) + donepezil hydrochloride (3 mg/kg).	17.46 ± 1.95[ab]	0.51 ± 0.04[d]	8.09 ± 0.36[c]	0.71 ± 0.09[b]	26.66 ± 2.37[b]

Table 3: Levels of brain hippocampus thiobarbaturic acid reactive substances (TBARS), acetylcholine (ACh), reduced glutathione (GSH) contents as well as acetylcholine esterase (AChE), monoamine oxidase (MAO) activity in normal and experimental groups of mice.

Values represent the mean ± SE (n = 6). Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05.

Groups	Treatment Description	Ca^{+2}-ATPase (U/mg protein)	Mg^{+2}-ATPase (U/ mg protein)	Na^{+}, K^{+}-ATPase (U/ mg protein)	Aβ1-42 (pg/mg protein)
I	Normal control (5 mL saline)	164.87 ± 6.87[e]	117.50 ± 10.77[d]	132.98 ± 18.75[d]	47.87 ± 5.26[a]
II	Scopolamine hydrobromide (SCO) (3 mg/kg.b.w.)	76.45 ± 5.33[a]	93.89 ± 5.32[a]	64.09 ± 8.44[a]	135.04 ± 10.45[d]
III	SCO (3 mg/kg.b.w. i.p.) + J. montana ethanolic extract (150 mg/ kg b.w.)	143.00 ± 12.86[c]	112.52 ± 8.00[c]	124.37 ± 10.66[c]	55.26 ± 4.37[b]
IV	SCO (3 mg/kg.b.w.i.p.) + donepezil hydrochloride (3 mg/kg.	122.65 ± 12.90[b]	106.88 ± 11.25[b]	110.87 ± 9.80[b]	63.53 ± 3.77[c]
V	SCO (3 mg/kg.b.w.) + J. montana ethanolic extract (150 mg/kg b.w.) + donepezil hydrochloride (3 mg/kg).	150.66 ± 11.54[d]	115.40 ± 13.29[cd]	128.73 ± 14.63[c]	46.75 ± 4.88[a]

Table 4: Levels of brain hippocampus Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activity as well as β amyloid1-42 level in normal and experimental groups of rats.

Values represent the mean ± SE (n = 6). Data shown are mean ± standard deviation of number of observations within each treatment. Data followed by the same letter are not significantly different at P ≤ 0.05.

Histopathology examination

Histopathological examination of brain hippocampus sections of the normal group (I). On the other hand, in the brain hippocampus of SCO-treated control group (II), histological examination showed amyloid plaques seen in Alzheimer (arrow).

Also, J. Montana ethanolic extract (150 mg/kg b.w.) and donepezil hydrochloride (3 mg/kg, orally) treated group (III and IV) demonstrated few amyloid-like plagues are seen, the arrow. Gliosis is also noted in brain hippocampus.

Histopathological examination also showed good recovery of SCO-induced brain hippocampus toxicity by administration of J. Montana ethanolic extract and donepezil hydrochloride group (V) in combination as compared with the SCO-treated group.

Discussion

In the present study, 14 days of SCO-administration has been found to elevate oxidative stress level in rat brain and also increased the neuroinflammatory in the hippocampus and plasma cholesterol, triglycerides and cholesterol-high density lipoprotein (HDL) as well as decrease brain hippocampus phospholipids levels. Our results in confirmed with the reports and evidence supporting the theory that oxidative stress plays a major role in the pathogenesis of neurodegenerative disease [42,43].

Also, accumulation of ROS in cells; a process previously implicated in the development of many Neurodegenerative diseases including Parkinson's disease, Huntington's disease, Amyotrophic lateral sclerosis and Alzheimer's disease [44,45]. Furthermore, a consistent neuropathological occurrence associated with memory loss is a cholinergic deficit, which has been correlated with the severity of Alzheimer's disease.

AChE inhibition has been reported to ameliorate the symptoms of some NDDs and has been used as a rationale to develop drugs to treat AD [46].

J. Montana ethanolic extract are well known to be a rich source of polyphenols like quercetin and to exhibit high antioxidant capacity [32,33]. Besides that, like many polyphenols of the J. Montana they are increasingly been attributed with a significant potential for human health benefits [32,33] and, in particular, quercetin have been reported to enhance short-term memory performance in animal models [47].

Here we investigated thiobarbaturic acid reactive substances (TBARS), acetylcholine (ACh), reduced glutathione (GSH) contents as well as acetylcholine esterase (AChE), monoamine oxidase (MAO) and comparatively studied the effects of different fatty acid composition of PC on brain function. Scopolamine, a traditional anti-cholinergic drug, is reported to have the capability of impairing spatial learning and memory and influencing the formation of short-term memory [48].

The rats with intake of J. Montana acquired better amelioration of oxidative stress. Interestingly, we found that J. Montana was effective on enhancing the GSH levels in hippocampus and the situation was reverse in cortex.

Also, MAO involved in amine metabolism found with high level in the brain [49]. It has been discovered to closely relate to the impairment of neural functions in central nervous system [50]. The ROS, generated by the reactions of MAO and neural transmitter, could combine with Fe^{2+} and then free radicals were created which promotes the damage of neurone [51]. An increase of MAO activity was detected in the brains of patients with AD [52].

In the present study, SCO reduced brain hippocampus Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activity as well as induced β amyloid1-42 levels. MAO has the ability of increasing the expression of β-secretase and γ-secretase and improving β amyloid1-42 generation [53-55] and could be also related to the formation of neurofibrillary tangles [56,57] when be activated.

In this context, several studies have reported that SCO exposure is associated with changes in important enzymes of CNS including AChE and Na^{+}, K^{+}-ATPase [58,59]. In addition, SCO can produce impairment of attention, learning and memory as well an increases in the aggressive and anxiogenic-like behavior [60,61].

The results of the present study demonstrated a significant increase in AChE activity in brain hippocampus from SCO-exposed rats lead to a fast ACh degradation and subsequent reduction of stimulation of ACh receptors causing undesirable effect on cholinergic neurotransmission as well progressive cognitive impairment.

Although other studies in humans [62] and rats [63] demonstrated sustained inhibitory effects of donepezil on AChE, the effective concentration of donepezil resulting in improved efficacy in the brain.

The alteration of MAO activity in brain hippocampus indicated that the supplemental J. Montana ethanolic extract had effectively decreased the MAO levels. It is recently reported that 14 days' intragastric administration can significantly normalize Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activity as well as β amyloid1-42 levels [64].

High content of flavonoids and phenolic compounds was found in Jasonia montana such as polyphenols [65-67]; 3,6,7,3`,4`- pentamethoxy quercetin (artemitin), 3,6,7,3`-tetramethoxy quercetin (chrysosplenetin), 3,6,3`,4`tetramethoxy quercetin, 3,6,7- trimethoxy kaem-pferol, 3,6,3`-trimethoxy quercetin (jaceidin), 3,6,4`trimethoxy quercetin (centaureidin), 3, 3, 4` trimethoxy quercetin, 3,6-dimethoxy quercetin, 3,3`-dimethoxy quercetin, 7,4`-dimethoxy quercetin, quercetin, quercetin-3-O-α-D-4C1- lucopyranoside, 3,5- dicaffeoyl-quinic acid, caffeic acid, quercetin-3-OL-1C4- rhamnopyranoside (Quercitrin) and quercetin-3- O-α- D-4C1 glucuronopyranoside which may be responsible for free radical activity. There are eighteen phenolic quercetin derivatives were isolated from the chloroform, ethyl acetate and n butanol fractions of Jasonia montana [68].

Quercetin is a strong antioxidant due to its ability to scavenge free radicals and bind transition metal ions. These properties of quercetin allow it to inhibit lipid peroxidation [69,70]. Lipid peroxidation is the process by which unsaturated fatty acids are converted to free radicals via the abstraction of hydrogen. Quercetin The subsequent free radicals are oxidized by molecular oxygen to create lipid peroxy radicals. This process is propagated by the resulting lipid peroxy radicals extracting hydrogen from other unsaturated fatty acid molecules to create more free radicals. It is catalyzed, in part, by the presence of trace amounts of transition metal ions. Lipid peroxidation can create deleterious effects throughout the body, such as cardiovascular and neurodegenerative diseases; however, it can be terminated by antioxidants, like quercetin, which interfere by reacting with the radicals formed [71].

It is known that quercetin can be accumulated enough in the CNS [72] and exhibits numerous actions on multiple biological targets that need to be further investigated. It is important to note that, in many situations, antioxidant effects comprise its most well-accepted pharmacological role and it is certainly responsible for several other effects of quercetin [73].

J. montana ethanolic extract and donepezil hydrochloride treatment almost normalized these effects in the histoarchitecture of the brain hippocampus. Furthermore, the histological changes in the brain hippocampus of rats treated by SCO. Therefore, the obtained biochemical, molecular biology and histological results of our study proved the JMEE could be a brain protective activity against SCO induced dementia in rats. In addition, the most novel and relevant finding was that JMEE and DHC supplementation was accompanied by the alleviation of brain proliferation, oxidative stress and inflammatory reaction in this model. The combination treatment of JMEE and DHC was also able to reduce newly formed brain tissues (Figure 1). The histological results were related to the biochemical parameters which estimated in the present study.

Figure 1: (a-e): Histological examination of different brain hippocampus tissue samples.

In addition, the prevention in the increase of AChE and MAO activity as well as β amyloid1-42 level in SCO-intoxicated rats by quercetin treatment may contribute to a maintain the levels of adenosine, which acts as an important neuroprotective molecule, so the treatment with quercetin can attenuate the neurological effects reported in cases of SCO-induced neurodegenerative. Prophylactic effect of JMEE in combination with DCH against SCO-induced dementia in rats has not been reported earlier to my knowledge, and this study is perhaps the first observation of its kind.

Conclusion

Our results demonstrate alterations in AChE, MAO, Ca^{+2}, Mg^{+2} and Na^{+}, K^{+}-ATPase activity as well as β amyloid1-42 level in brain hippocampus of SCO-exposed rats. Interestingly, J. Montana ethanolic extract treatment prevented totally or partially this effects caused by SCO-exposure. Therefore, reactivity of polyphenols as reflected in their antioxidant potential means that certain quercetin derivatives can bind with proteins impacting their behavior in cholinergic and purinergic system on SNC. We can suggest that J. Montana ethanolic extract is a promising candidate among the medicinal plants to be investigated as a therapeutic agent, and thus be used to attenuate neurological disorders associated with SCO-induced neurodegenerative.

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