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The Improvement Potential of Camel Milk Whey as a Natural Remedy in Comparison with Rivastigmine Chitosan-Loaded Nanoparticles in Aluminum Chloride Induced Alzheimer-Like Disease in Rats

Dina E. ElMosbah [1]*, Marwa S. Khattab[1], Marwa A. Ibrahim[2], Heba M.A. Khalil[3], Mona I. El-Asssal[4] and Hala M.F. El Miniawy[1]

[1] *Department of Pathology, Faculty of Veterinary Medicine, Cairo University, Giza, 12211, Egypt.*

[2] *Department of Biochemistry and Chemistry of Nutrition, Faculty of Veterinary Medicine, Cairo University, Giza, 12211, Egypt.*

[3] *Department of Veterinary Hygiene and Management, Faculty of Veterinary Medicine, Cairo University, Giza, 12211, Egypt.*

[4] *Department of Pharmaceutics and Pharmaceutical Technology, Faculty of Pharmacy, Future University in Egypt, 11835, Cairo, Egypt.*

Abstract

THE most prevalent long-term neurodegenerative illness is Alzheimer's disease (AD). Worldwide, there are more than 24 million cases of AD, making the development of effective treatments imperative. The probable therapeutic potential of camel milk whey as a natural intervention and Rivastigmine loaded nanoparticles was investigated in this study. Alzheimer's like disease model was established by giving rats 100 mg/kg/b.wt. of aluminum Chloride orally for 3 months. Then the experimental rats were treated either with camel milk whey or Rivastigmine loaded nanoparticles for 75 days. Behavioral tests, histopathology, immunohistochemistry of Tau and Sirt-1 expression in addition to gene expression of TNF-α, MAO-A, Nrf-2 and VEGF1 in brain tissue were performed. Camel milk whey and Rivastigmine-loaded nanoparticles improved cognitive decline and regulated the expression of TNF-α, MAO-A, Nrf-2, VEGF1 and Tau in brain tissue. Interestingly, treatment groups showed increased expression of Sirt-1 in neurons, which may influence several facets of hippocampus and cortical cell survival and function, thereby altering the progression of the disease. Consequently, both therapies blocked the inflammatory cascade and alleviated the neurodegenerative lesions encountered in AD with better results in the group treated with Rivastigmine loaded nanoparticles.

Keywords: Camel whey, Rivastigmine nanoparticles, Tau, Sirt-1, TNF-α.

Introduction

Alzheimer's disease (AD), a neurodegenerative disorder, affects memory, thinking and behaviors adversely [1]. AD is currently the sixth prevalent reason of death worldwide. AD characteristics involve amyloid β-peptide (Aβ) and hyperphosphorylated tau protein precipitation, inflammatory mediators release and synaptic, cholinergic, and cognitive lowered functions [2]. The constant exposure to aluminum chloride ($AlCl_3$) causes neurotoxicity with subsequent oligomerization of amyloid β-protein which qualifies it to be an inducer of AD [3,4].

Although the efficiency of existing AD treatments remains limited, some drugs as donepezil, rivastigmine, memantine and galantamine can only alleviate neurological symptoms briefly without reversing or halting the neurological lesions [5,6]. This could be due to the inadequate availability of the drug in the brain tissue and its limited Blood Brain Barrier crossing [7]. Because of this, the

*Corresponding author: Dina Emad ElMosbah, , E-mail: dinaemadeldeen@cu.edu.eg , Tel.: 01025308841
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administrated dosage is increased leading to undesired effects. Many other side effects are incriminated with these drugs as the high cost and unsuitability for all AD patients. Research is being conducted to evaluate novel approaches for improving the molecules' bioavailability to the brain with efficient delivery. The utilization of nanoparticles (NP), 10 and 1000 nm, would overcome the BBB allowing effective targeting of therapeutic molecules to brain [8,9].

Remedies of natural origin are being investigated in the treatment of several chronic diseases due to its lower side effects. Camel milk (CM) possesses numerous therapeutic benefits, including antiviral, antifungal, antibacterial, antioxidant, hypoglycemic, anti-inflammatory and anti-cancer activities. These benefits are mainly accredited to the presence of high vitamin C and Camel whey protein (CWP) in CM [10,11]. CWP is deemed a powerful natural antioxidant since it improves immunity, lowers oxidative stress, and elevates antioxidants. It encompasses various active constituents, like lactoglobulins, immunoglobulins, lactoferrin (LF), lactoperoxidase, lysozyme, and α-lactalbumin [12]. Moreover, CWP reduces oxidative stress, protects neurons, and improves the neurobehavior of diabetic mice [13].

Hence, in the existing study, neurobehavioral, molecular, and neuropathological assessments were performed to evaluate if camel whey as natural dietary supplement could provide therapeutic potency against $AlCl_3$ induced AD in comparison with Rivastigmine-loaded nanoparticles.

Materials and Methods

Animals

Rats used in this study were males, albino and weighed 200–250 g. They underwent acclimatization for a week after being housed in plastic cages containing sawdust. The conditions were maintained at 25 ± 2 °C temperature, 12/12 hours light-dark cycle, and water and food freely available. Animals were monitored for any distress or behavioral alterations.

Ethical approval

The Institutional Animal Care and Use Committee (Faculty of Veterinary Medicine, Cairo University) approved this study with No. vet Cu 23052022454.

Determination of Protein fraction of camel milk

Defatted milk was prepared by removing milk fat after being centrifuged for 30 min at 5000 rpm, followed by filtration through Gauze. The resultant milk was treated using the technique of Moatsou et al. [14]. The whey and casein proteins were kept at -28 C until subjected to fractionation using Reverse-phase high-performance liquid chromatography (HPLC) (Waters Corp., USA). The software Breeze version 3.30 SPA was used to process data. The separation of samples was carried out on a reversed-phase analytical column Symmetry C4, 150 x 4.6 mm, 5µm particle size, and 300-A pore size [15].

Preparation of camel whey

Casein of camel milk was precipitated at pH 4.3 using 20% acetic acid, and then the supernatant was collected after centrifugation at 3000 rpm for 20 minutes as whey according to the method provided by Salami et al. [16].

Rivastigmine-loadednanoparticles preparation.

Desperation of Rivastigmine (RS) harbored on optimized chitosan nanoparticles as polymeric Nano-carriers was prepared. The formulation of chitosan nanoparticles (CSNPs) was done by ionotropic gelation of chitosan using sodium tripolyphosphate STPP anions [17]. The detailed preparation procedures with some methodology modification and the choices of the optimal formula have been explained in previous published research [18]. The optimized loaded RS-CSNPs desperation were evaluated in vitro [18].

Experimental design

Twenty rats were allocated into 2 major groups: G1, the rats were given distilled water orally per day, acting as a control negative group. G2, rats were orally administrated $AlCl_3$ (100 mg/kg/b.wt daily) for 90 days to induce AD (confirmed by behavioral tests) [19]. After that, G2 were subdivided into 3 subgroups of 5 rats each as follows: G2a ($AlCl_3$ group), kept as positive control group, G2b (Whey group), rats were treated with 3 ml camel milk whey daily for 75 days [20,21], G2c (Rivastigmine group), rats were treated orally with 1ml Rivastigmine (RS) loaded on chitosan nanoparticles (containing 0.13 mg Rivastigmine) daily for 75 days [22].

Behavioral test

Rats were submitted to the behavioral analysis room at the termination of the study. They were acclimatized to the presence of the experimenter for 3 hrs., and then tested using two behavioral tests as follows:

1. Elevated plus maze

Rats were evaluated for their anxiety like behavior in the elevated plus maze [23].

2. Y-maze test

Rats were then tested for their working spatial memory directly after the open field test. Y-maze is composed of three identical arms shaping the letter

(Y). The rat was positioned in one arm of these three arms and observed for 5 min. The arm entries number and the percent of spontaneous alternation indicating the rats capability to switch between three variable arms and it was calculated from the following equation: The spontaneous alternation percentage (SAP %) = [(number of alternation)/(total arm entries-2)]x100% [24].

Histopathological examination

The brain specimens were processed after fixation in 10% neutral buffered formalin using ethanol and xylene. Tissues were embedded in paraffin wax, sectioned (3–4 µm thick), and stained with hematoxylin and eosin (H&E) [25]. Light microscopy was used for examination. The incidence and severity of the following alterations: neuronal degeneration, Gliosis, Vascular changes, Hippocampus cellular loss and Vacuolation were scored as (0) absent, (1) minimal, (3) mild (2) moderate, and (3) severe lesions [26].

Immunohistochemistry (IHC)

The phosphorylated tau and Sirt1 immunohistochemistry in the brain were performed. Antigen retrieval using citrate buffer was carried out after deparaffinization and rehydration. The phosphorylated tau (abx328322, Abexxa, UK) and Sirt1 (13161-1-AP, Proteintech, Germany) primary antibody at dilution of 1:100 was applied to slides followed by the secondary antibody (Vactastain ABC peroxidase kit, Vector Laboratories, Burlingame, CA, USA). Chromogen 3, 3-diaminobenzidine tetrahydrochloride (DAB, Sigma Chemicals, Perth, Australia) was used as substrate and hematoxylin as counterstain [27]. The positive area percent mean of Tau and Sirt1 in brain was measured at magnification power 200X /rat in 10 fields by Image J software.

Gene expression evaluation

Total RNA was extracted by Qiagen mini-RNeasy extraction kit, based on the manufacturer's protocol. The purity and concentration of RNA were determined by spectrophotometry at wavelengths 260 and 280 nm [28]. Subsequently, the Revert Aid First Strand cDNA Synthesis Kit (Thermo Scientific) was used to create complementary DNA (cDNA) after treating the samples with DNase I to remove DNA contamination (Fermentas, Lithuania).

To detect the mRNA levels of specific genes, primer sets were designed using the Rattus Norvegicus sequences available in Gen Bank (Table 1). The relative expression of the target genes was evaluated by real-time PCR analysis and SYBR Green PCR Master Mix. ABI Prism Step One Plus Real-Time PCR System was used for real-time PCR. Each sample was subjected to two PCR runs. The expression levels of the studied genes were normalized using housekeeping gene beta-actin (*β-Act*). The gene expression data were evaluated using the DDCt technique [29].

Statistical analysis

The statistical package version 8.0 (SPSS Inc., Chicago, IL, U.S.A.), was used to perform the statistical analysis. ANOVA was used to evaluate parametric data, and Duncan and Tamhane's post hoc tests were conducted after the homogeneity of variance test. The lesion score significance at P values less than 0.05 was assessed by the Kruskal-Wallis test followed by Mann Whitney test.

Results and Discussion

Analysis of Protein fraction of camel milk: it was depicted in table (2).

Behavioral assessment

The number of arm entries recorded no significant difference between $AlCl_3$ intoxicated rats and control group. Concerning SAP, the $AlCl_3$ rats recorded a declined SAP in comparison to control group. While, whey and Rivastigmine treated rats exhibited a substantial rise in the SAP in comparison to $AlCl_3$ rats. Regarding the elevated plus maze test, the open arm frequency and duration, and closed arm frequency and duration were significant between groups. $AlCl_3$ intoxicated group showed a substantial decrease in the frequency of open arm entry with a marked rise in the closed arm entry in comparison to control group. Conversely, whey and Rivastigmine treated rats displayed a significant elevation in the frequency of open arm entry associated with a marked decrease in the closed arm entry in comparison to $AlCl_3$ intoxicated group. Moreover, $AlCl_3$ intoxicated group displayed a substantial reduction in the open arms interval and marked increase in the closed arms duration in comparison to control group. Conversely, Rivastigmine administered rats presented a rise in the open arm period with a decrease in the closed arm period in comparison to $AlCl_3$ intoxicated group. Although, whey supplied rats showed an elevation in the open arm duration associated with a decrease in the closed arm duration compared to $AlCl_3$ intoxicated group but it was insignificant as shown in table (3).

Histopathological examination

Microscopy of the brain revealed typical histological structure of different regions. In the $AlCl_3$ group, lesions observed were coinciding with AD in different brain regions. Vasculitis and blood vessel thickening were observed with the presence of minute foci of hemorrhage in some tissue sections primarily in the striatum and midbrain. Marked astroglial and microglial reactions associated with neuronal degeneration and neuronophagia. The hippocampus had an abnormally appearing cells with flame shaped processes especially in Cornu Ammonis 4 and decreased their cellular density.

Vacuolation of neuropil and demyelination were observed especially in the striatum region. In contrast, rats treated with whey and Rivastigmine exhibited moderate histological alteration with no hemorrhage observed and vascular injury compared to $AlCl_3$ intoxicated group (Fig.1). The severity of lesion among different groups was indicated by scoring as shown in Fig.2.

Immunohistochemistry investigation

Tau expression was widely expressed in neurons in different brain regions. Its' area percent was meaningfully elevated in the $AlCl_3$ administered rats. There was a noteworthy decline of the expression in Rivastigmine treated rats in comparison to whey treated group (Fig.3).

Sirt-1 expression was widely expressed in nerve cells of hippocampus and cerebral cortex. Its' area percent remarkably lessened in the $AlCl_3$ administered rats but was partially elevated in treated groups especially the Rivastigmine group (Fig.3).

Genetic analysis

The gene expression results revealed a significant overexpression in the TNF, MAO-A and VEGF1 and downregulation of Nrf-2 genes in the $AlCl_3$ group compared to other groups. Additionally, rats treated with Rivastigmine showed significantly lower levels of TNF, MAO-A, and VEGF1 expression, whereas Nrf-2 gene expression was higher than in groups treated with whey (Fig.4).

Discussion

The development of effective treatment against AD is one of the biggest difficulties facing the profession of neurology [30]. The ameliorative possibility of camel whey and Rivastigmine NPs against AD induced by $AlCl_3$ in rats was investigated in this study. Many studies reported that $AlCl_3$ could induce neuropathological hallmarks of AD which mimic those that occur in humans [31,32].

Current studies evaluate cytokine-mediated neuroinflammation as a primary reason in the onset of AD. Cytokines implicated in neuroinflammation includes mainly tumor necrosis factor alpha (TNF-α) [33]. Our findings recorded a substantial rise in TNF-α expression in the $AlCl_3$ group. Higher TNF-α levels have a role in AD as they promote Aβ production, lowers Aβ clearance, induce tau-related pathology and increase neuronal death [34]. Additionally, TNF-α causes neuroinflammation in the hippocampus with subsequent memory and spatial learning hindrance and eventually cognitive deterioration [35,36]. This was evident in our behavioral findings. Therefore, TNF inhibitors was approved by FDA for treating AD although it can't cross the BBB easily due to their large sized molecules [34]. In this study, A remarkable reduction in TNF-α expression in rats receiving Rivastigmine NPs was recorded which could be attributed to nanotechnology as it aids in effective drug delivery to the brain [37]. Moreover, camel whey alleviated AD by decreasing the TNF-α level in the brain as it contains bioactive components such as lactoferrin, lysozyme, and lactoperoxidase which have anti-inflammatory activities [38].

Nrf-2 act as a protagonist in keeping cellular redox homeostasis and modification of inflammatory response. Nrf-2 expression also offers neuroprotection in neurodegenerative diseases [39]. In this study, the Nrf-2 gene expression level is significantly increased in rats treated with either camel whey or Rivastigmine NPs compared to rats that received $AlCl_3$. This evidence implies that Nrf-2 could be an innovative therapeutic possibility for AD. Previous data showed that Nrf-2 hinders various crucial points in AD pathogenesis like phosphorylated tau (p-tau) and Aβ pathways. Nrf2 elevation in AD can amend cellular injuries induced by reactive oxygen species and mitochondrial dysfunction [40,41].

Activated monoamine oxidase (MAO) is crucial to AD pathophysiology [42]. The relationship between oxidative stress and MAO activation in AD is widely recognized as a cause of neurotransmitter dysfunction, specifically in the adrenergic and cholinergic systems, which is crucial for cognitive decline [43]. The connection between oxidative stress and neuroinflammation is a critical factor in Aβ production, where MAO may serve like a proinflammatory cytokine. The therapeutic approaches that target the aforementioned two pathways could be beneficial. MAO inhibitors would reduce the formation of Aβ by impeding neuroinflammation via downregulating the expression of TNF-α, and interleukin-1β in addition to reducing glial activation [44].

Sirt-1 belongs to sirtuin family which uses nicotinamide substrate to catalyze the deacetylation of variable substrates and have beneficial effects against AD [45]. The impedance of Sirt-1 activity prevents tau polyubiquitination with consequent buildup of p-tau in nerve cells. In the present work, rats in $AlCl_3$ group showed a marked reduction in Sirt-1 expression and an elevation in tau expression, unlike rats in groups treated with camel whey and Rivastigmine NPs. Previous research reported that Sirt-1 reduction was correlated to tau accumulation in AD [46] as it is important in regulating the deacetylation of p-tau, and the production of proinflammatory cytokines and ROS in the brain [47,48]. The dissociation of p-tau was found to enhance cognition and decrease neuronal death [47].

Sirt-1 is important for synaptic plasticity and cognition so its expression diminution in hippocampal nerve cells is linked with impaired cognition like spatial learning and memory [49].

Therefore, the activation of Sirt-1 could hinder further Aβ precipitation and AD neurodegeneration [50]. Likewise, to our findings, Ubaid et al. reported that α-lactoalbumin component of camel whey is capable of increasing Sirt-1 expression in an induced model of Parkinson's disease [51].

Our histological findings validated the neurotoxic effect of $AlCl_3$ in different brain region with severe vascular alteration including vasculitis and blood vessels thickening. This was associated with over expression of vascular endothelial growth factor 1 (VEGF1). This overexpression in response to exposure to $AlCl_3$ raises the possibility that aluminum could cause an increase in VEGF1 synthesis. This increase could be an adaptive reaction to aluminum toxicity's after impairment of blood vessel function. In this context, the activation of local endothelial cells inflammatory cytokines allows recruitment of leukocytes to the place of injury prompting stalled capillaries, and ultimate reduction in cerebral blood flow [52]. Upregulation of the VEGF1 was previously reported following brain injury and in AD [53].

Furthermore, elevated VEGF expression in the AD brain have been linked to loss of pericytes, and increased vascular and BBB permeability leading to brain edema [54]. In the present study, both treatments downregulate VEGF indicating the decrease of its detrimental effects on the BBB and more advantageous outcomes. This result agrees with the previously reported improvement of induced Parkinson's illness in mice after inhibition of VEGF [55]. Previous data reported also that camel milk decreased VEGF factor in mice [56].

Conclusions

Based on the study data, it may be inferred that camel whey as a natural dietary supplement and Rivastigmine-loaded chitosan NPs have a mitigation effect in the experimental AD model. The Rivastigmine-loaded chitosan NPs outperformed the camel whey. Both therapies improved cognitive impairment and regulated TNF-α, MAO, Nrf-2, VEGF1 and Tau expression in addition to activation of Sirt-1 expression in neurons. Therefore, they represent a promising approach for AD management which requires further clinical research.

Conflicts of interest

The authors declare no conflict of interest.

Funding statement

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TABLE 1. The sets of primers used in the study

Gene	Forward	Reverse	Product size	Accession number
TNF-α	ACACACGAGACGCTGAAGTA	GGAACAGTCTGGGAAGCTCT	235	NM_012675.3
Nrf-2	TGTAGATGACCATGAGTCGC	TCCTGCCAAACTTGCTCCAT	159	NM_031789.2
MAO-A	GTG CCT GGT CTG CTC AAG A	GGC CCA AAC CAT AGG CTG TA	168	NM_033653.1
VEGF1	GCAATGATGAAGCCCTGGAG	GCTTGTCACATACGCTCCAG	158	NM_012922.2
β- Act	CCGCGAGTACAACCTTCTTG	CAGTTGGTGACAATGCCGTG	297	NM_031144.3

TABLE 2. Milk protein fraction of camel milk (mg/l milk)

Exam. parameters	Case No. 1	Case No. 2	Case No. 3	Case No.4	Case No. 5	Mean	± SD
α-Casein	7160	6943	7154	7150	7148	7111	94.03
α-S1 casein	5000	4826	4896	4968	4985	4935	72.83
α-S2 casein	2200	2170	2190	2200	2210	2194	15.17
β-casein	15000	14980	15000	14990	14970	14988	13.04
κ-casein	800	806	801	800	800	801.4	2.61
α-Lactalbumin	3500	3499	3500	3500	3500	3499.8	0.45
β-Lactglobulin	250	260	240	248	255	250.6	7.54
Lactoferrin	580	490	530	480	620	540	59.58

TABLE 3. Effect of camel whey and Rivastigmine loaded nanoparticles administration on spatial working memory and anxiety like behaviour of $AlCl_3$ intoxicated rats

	Group	N	Mean		SD	SE
Number of arms	Control	6	7.00		0.894	0.365
	$AlCl_3$	6	5.83		0.753	0.307
	whey	6	6.00		1.722	0.703
	Rivastigmine	6	7.17		0.894	0.365
SAP	Control	6	81.67		10.698	4.367
	$AlCl_3$	6	34.44	*	9.526	3.889
	whey	6	59.44	*@	13.239	5.405
	Rivastigmine	6	61.03	*@	11.627	4.747
Open arm frequency	Control	6	5.33		1.366	0.558
	$AlCl_3$	6	2.33	*	1.211	0.494
	whey	6	6.67	@	1.366	0.558
	Rivastigmine	6	6.83	@	0.983	0.401
Open duration	Control	6	193.83		16.975	6.930
	$AlCl_3$	6	65.00	*	10.488	4.282
	whey	6	100.50	*	77.195	31.515
	Rivastigmine	6	160.67	@	46.805	19.108
Closed arm frequency	Control	6	2.50		0.548	0.224
	$AlCl_3$	6	4.00	*	0.894	0.365
	whey	6	3.50	*	0.753	0.307
	Rivastigmine	6	2.83	@	0.548	0.224
Closed duration	Control	6	106.17		16.975	6.930
	$AlCl_3$	6	235.00	*	10.488	4.282
	whey	6	199.50	*	77.195	31.515
	Rivastigmine	6	139.33	@	46.805	19.108

* Indicates significance with control group; @ means significance with $AlCl_3$ group. $P<0.05$.

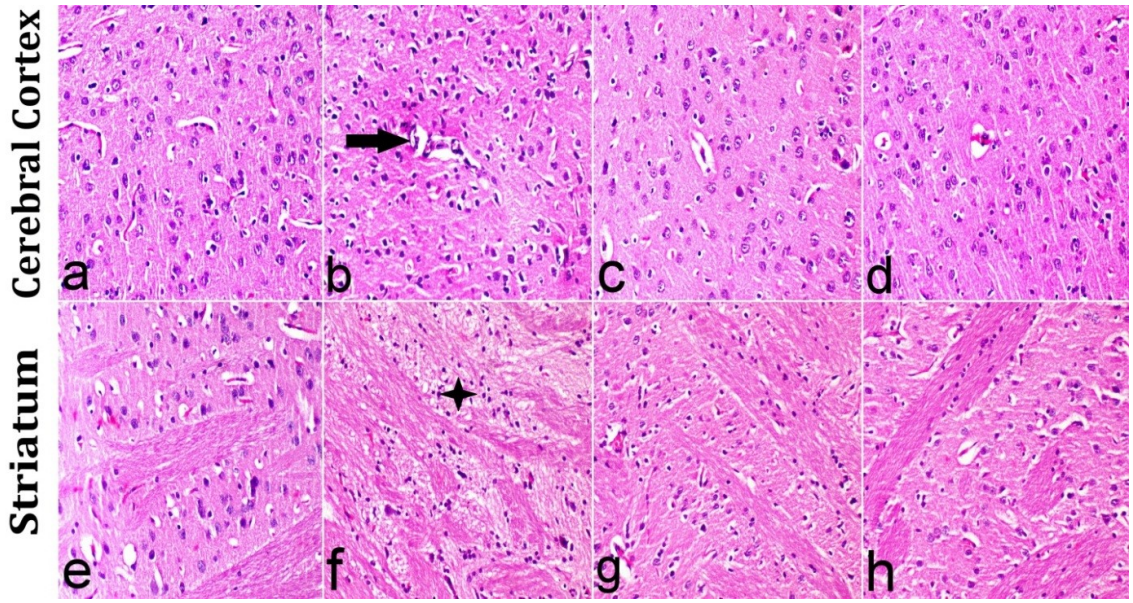

Fig. 1. Photomicrograph of rat brain, cerebral cortex and striatum region (H&E) stained; (a) Normal structure of cortex in control group, (b) Neuronal degeneration with gliosis and cerebral angiopathy (arrow) in $AlCl_3$ group, (c) and (d) showed few neuronal degeneration in whey group and Rivastigmine group respectively, (e) Normal structure of striatum in control group, (f) severe demyelination with gliosis (asterisk) in $AlCl_3$ group, (g) mild vacuolation of neuropil with mild glial reaction in whey treated group, (h) and in Rivastigmine treated group, 200x.

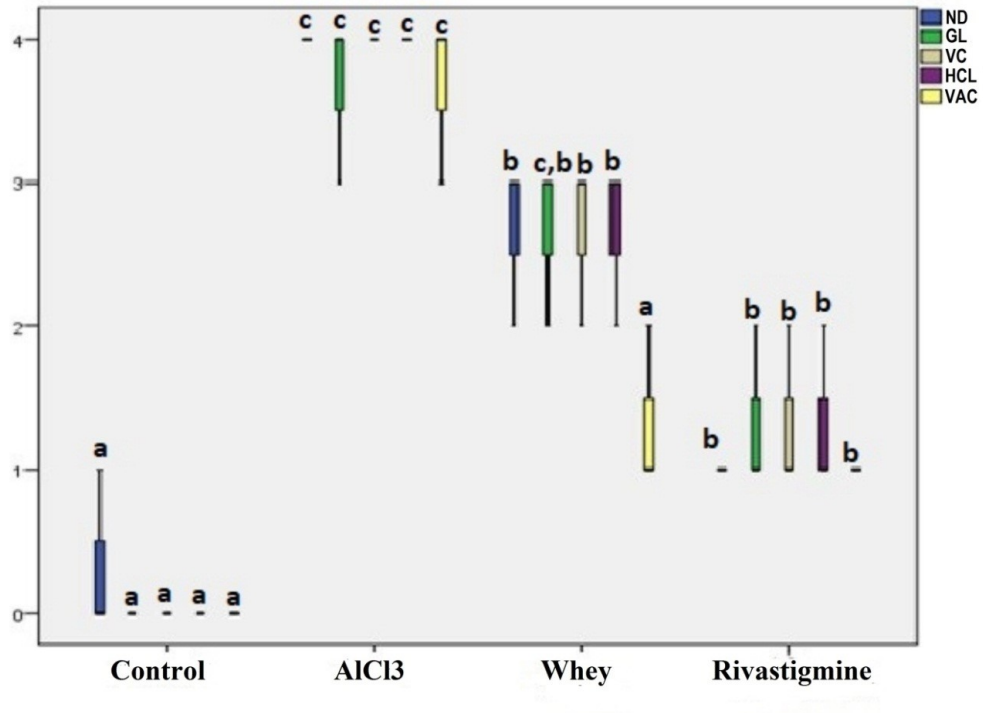

Fig. 2. Lesion scores of ND (neuronal degeneration), GL (Gliosis), VC (Vascular changes), HCL (Hippocampus cellular loss) and VAC (Vacuolation) in brain tissue in different groups. Boxes bearing different superscripts (a,b,c) are significant at P values less than 0.05, (n= 5).

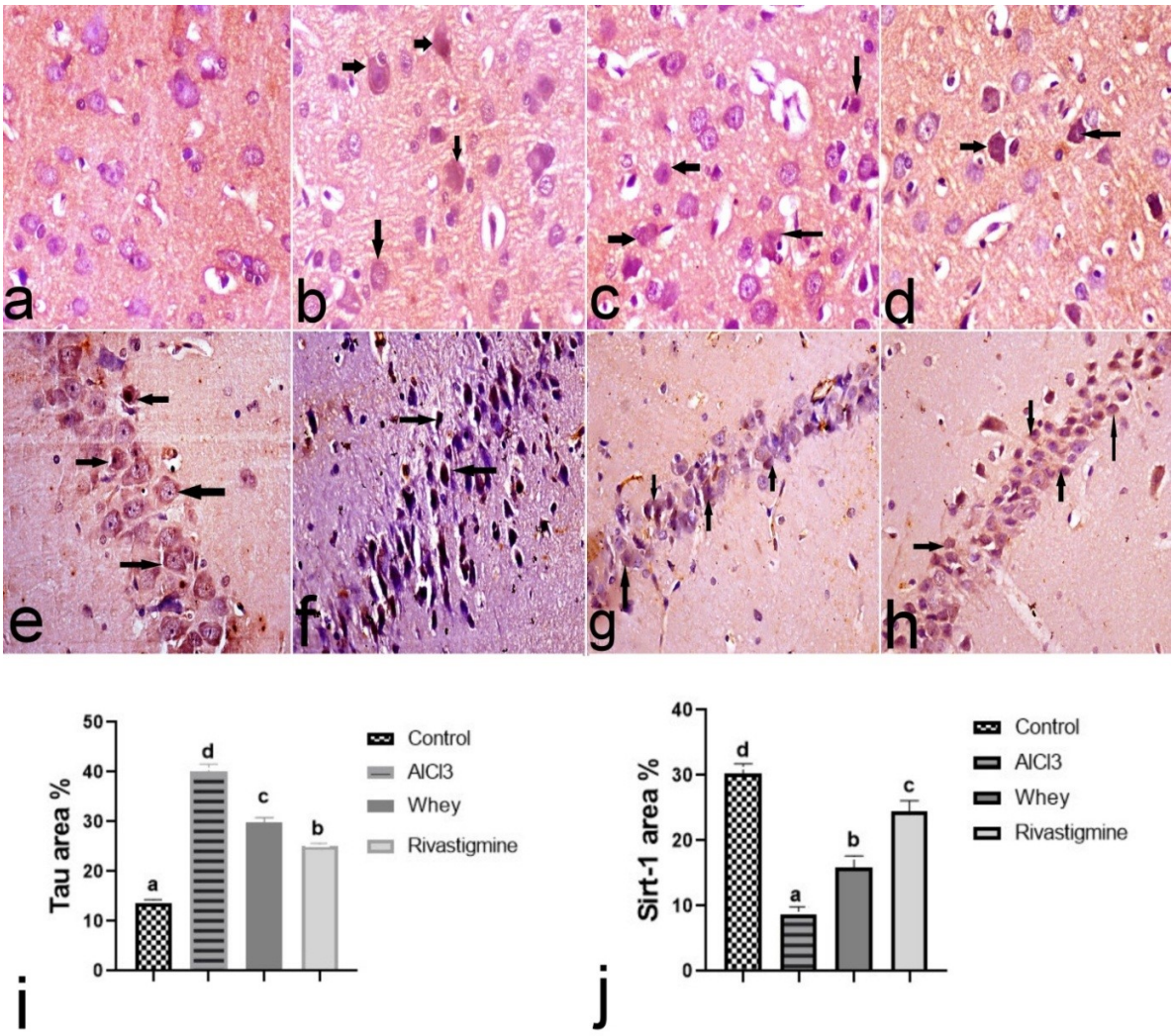

Fig. 3. Immunohistochemistry of Tau and Sirt-1 expression in brain tissue in different groups; (a) absence of Tau expression in the control group, (b) severe expression of Tau in the neurons in the $AlCl_3$ group (arrow), (c) mild expression of Tau in whey treated group, (d) and in Rivastigmine treated group (arrow), (e) Sirt-1 expression in hippocampal neurons of control group (arrow), (f) low expression of Sirt-1 in hippocampal neurons of $AlCl_3$ group (arrow), (g) high expression of Sirt-1 in hippocampal neurons of whey treated group, (h) and Rivastigmine treated group (arrow), 400x. (i) Tau expression significantly increased in the $AlCl_3$ group compared to other groups, (j) Sirt-1 expression significantly decreased in the $AlCl_3$ group compared to other groups. All data presented as mean± SE. Values bearing different superscripts (a,b,c,d) are significant at P values less than 0.05.

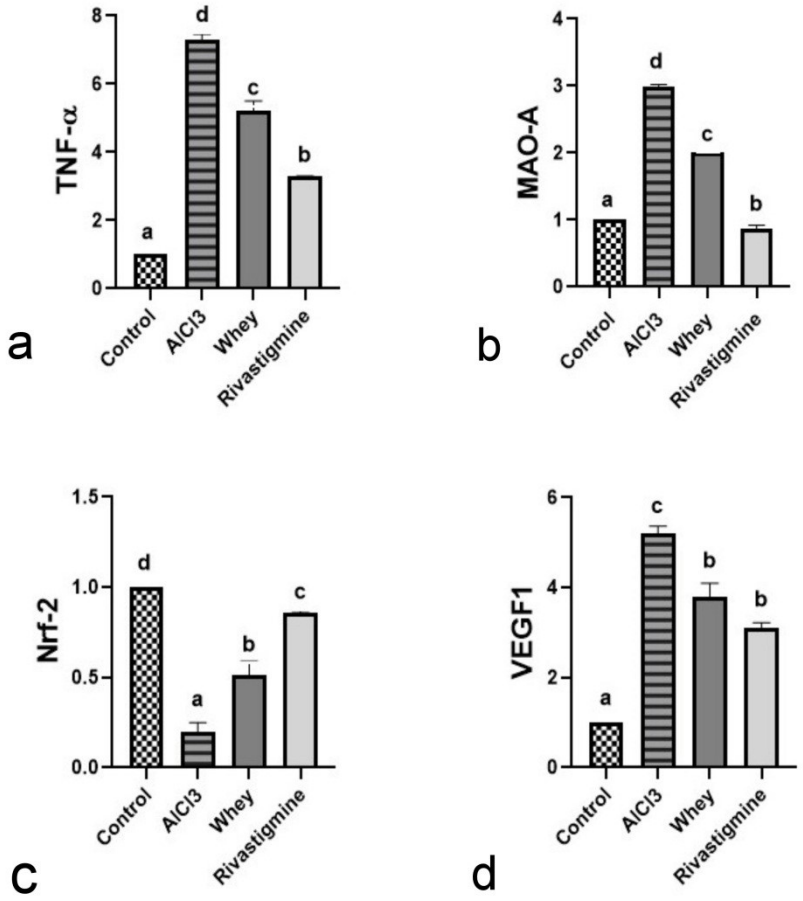

Fig. 4. Bar charts representing the fold changes of (a) TNF-α, (b) MAO-A, (c) Nrf-2 and (d) VEGF1 genes in the brain. Values are presented as mean ± SE, (n= 5) and different superscript letters indicated the significant differences between groups at P < 0.05.

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إمكانية تحسين مصل حليب الإبل كعلاج طبيعي بالمقارنة مع الجسيمات النانوية المحملة بالريفاستيجمين الشيتوزان في مرض الزهايمر المستحث بكلوريد الألومنيوم في الجرذان

دينا عماد المصباح[1] ، مروة صلاح خطاب[1] ، مروة إبراهيم[2] ، هبة محمد علي خليل[3] ، مني إبراهيم العسال[4] و هالة محمد فاروق المنياوي[1]

[1] قسم الباثولوجيا - كلية الطب البيطري - جامعة القاهرة - مصر.

[2] قسم الكيمياء الحيوية وكيمياء التغذية - كلية الطب البيطري - جامعة القاهرة - مصر.

[3] قسم الصحة - كلية الطب البيطري - جامعة القاهرة - مصر.

[4] قسم الصيدلانيات والتكنولوجيا الصيدلية - كلية الصيدلة - جامعة المستقبل - مصر.

يعتبر مرض الزهايمر من أكثر أمراض التنكس العصبي انتشارًا على المدى الطويل. في جميع أنحاء العالم، هناك أكثر من 24 مليون حالة من مرض الزهايمر، مما يجعل تطوير علاجات فعالة أمرا حتميا. تم في هذه الدراسة دراسة الإمكانات العلاجية المحتملة لمصل حليب الإبل كتدخل طبيعي والجسيمات النانوية المحملة بالريفاستيجمين. تم إحداث نموذج لمرض الزهايمر في الفئران عن طريق إعطاء الفئران 100 ملجم من كلوريد الألومنيوم لمدة ثلاث أشهر. ثم عولجت فئران التجارب إما بمصل حليب الإبل أو بجزيئات الريفاستيجمين النانوية المحملة . تم إجراء الاختبارات السلوكية والتشريح المرضي والكيمياء المناعية لتعبير Tau وSirt-1 بالإضافة إلى التعبير الجيني لـ TNF-α وMAO-A وNrf-2 وVEGF1 في أنسجة المخ. أدى مصل حليب الإبل والجسيمات النانوية المحملة بالريفاستيجمين إلى تحسين التدهور المعرفي و تنظيم تعبير TNF-α وMAO-A وNrf-2 وVEGF1 وTau في أنسجة المخ بالإضافة إلى زيادة في تعبير Sirt-1 في الخلايا العصبية. ونتيجة لذلك، كلا العلاجين لهم القدرة علي منع سلسلة الالتهابات وتخفيف حدة الآفات التنكسية العصبية التي تمت مواجهتها في مرض الزهايمر مع نتائج أفضل في المجموعة التي عولجت بالجسيمات النانوية المحملة بالريفاستيجمين.

الكلمات الدالة: مصل حليب الإبل والجسيمات النانوية المحملة بالريفاستيجمين وTau و Sirt-1 وTNF-α.