

The protective effect of MitoQ on A β 42 Induced Mitochondrial Dysfunction in SH-SY5Y Neuroblastoma Cells, An In Vitro Model of Alzheimer's Disease

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ABSTRACT

The rising incidence of neurodegenerative diseases, particularly Alzheimer's disease (AD), has paralleled increased human life expectancy, severely affecting patient quality of life and imposing a burden on healthcare systems. Mitochondrial dysfunction has been recognized as a critical factor in AD pathogenesis.

This study investigates the protective effects of MitoQ, a mitochondria-targeted antioxidant, on SH-SY5Y cells treated with amyloid-beta (A β 42), mimicking AD pathology.

Experimental in vitro study.

SH-SY5Y neuroblastoma cells were exposed to A β 42 to induce AD-like features, followed by MitoQ treatment. Markers of mitochondrial dysfunction were assessed, including reactive oxygen species (ROS) levels, mitochondrial membrane potential (MMP), and protein expression of antioxidant and mitochondrial-related genes (SODs, CAT, BACE2, ATPs, COIs, TRAKs, OPA1).

MitoQ significantly reduced ROS levels and restored MMP. It also upregulated antioxidant genes (SODs, CAT, BACE2) and OPA-1 expression, while downregulating ATPs, COIs, and TRAKs associated with mitochondrial stress.

We successfully created an Alzheimer's model utilizing A β 42 and studied the effect of the mitochondria-targeted antioxidant molecule, MitoQ, on oxidative stress and mitochondrial dysfunction in this work. We discovered substantial changes in gene and protein expression, as well as changes in mitochondrial membrane structure. These findings, together with MitoQ's possible therapeutic benefits, indicate the drug's potential as a treatment for Alzheimer's disease. Animal investigations are needed to corroborate these findings and get more accurate insights, especially in organs immediately impacted, such as the brain.

Keywords: Alzheimer's Disease, MitoQ, Mitochondrial Dysfunction, Neurodegeneration

Introduction

Neurodegenerative diseases give rise to dementia and cognitive disorders, mainly due to their impact on neurons. Neurons, which have limited glycolytic capacity yet possess a highly metabolically active structure, exhibit a substantial demand for energy. Meeting this energy requirement necessitates robust mitochondrial function. The precise positioning of mitochondria

within neuronal structures, coupled with accurate distribution and effective transport mechanisms, holds paramount importance in ensuring optimal mitochondrial functionality (1).

Mitochondria are often known as the 'powerhouses of the cell' because of their role in producing energy. These organelles, which have two membranes and their own genetic material, are present in all eukaryotic organisms and have a diameter ranging from 0.75 to 3 μ m. Cellular size

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and structure can differ based on functional requirements. Interestingly, mitochondria possess the ability to multiply in response to energy demands, a process independent of cell division (1, 2).

AD, the most prevalent neurodegenerative disorder, was initially documented by Alois Alzheimer, a German physician. Initially, his patient was diagnosed with a mental illness. However, upon her demise, Dr. Alzheimer observed the presence of plaque formation within her brain. Depending on the affected regions of the brain, individuals with AD exhibit varying symptoms that typically initiate with memory impairment. Over time, patients may also experience enduring memory loss, coupled with hallucinations triggered by disruptions in rational thinking and emotional responses. In advanced stages, AD can lead to fatality by impacting respiration and heart function. While no definitive cure exists, current therapies aim to decelerate the disease progression. AD is a complex ailment with a multifaceted origin, involving both genetic predisposition and environmental factors as risk elements (3).

Five hypotheses are considered valid explanations for the onset of AD. These include hereditary transmission, reduced acetylcholine synthesis, the neurotoxic impact of amyloid-beta ($A\beta$) accumulation in the brain, the formation of neurofibrillary tangles in the brain due to hyperphosphorylated tau, and impaired mitochondrial dynamics and functions. $A\beta$ plaques hinder neuronal communication, while tau tangles obstruct the intake of essential nutrients. Notably, early-stage AD exhibits mitochondrial dysfunction, which is believed to potentially underlie the disease's development. This insight raises the possibility of early disease detection and treatment strategies (4).

The amyloid precursor protein (APP) is a protein that is generated through proteolysis by enzymes called α -, β - and γ -secretases. α -Secretase cleaves the transmembrane region of APP, creating the α -APP fragment, which is located 12 amino acids from the cleavage site. Alternatively, the β -secretase enzyme cleaves closer to the amino terminus, generating the β -APPs fragment, only 16 amino acids away. Subsequently, γ -secretase performs a second cleavage. After α -secretase cleavage, a p3 fragment forms, while β -secretase cleavage produces the $A\beta$ peptide. Notably, the length of the $A\beta$ peptide is determined by the γ -secretase enzyme, which might be more active in cases of AD. An additional potential factor in AD

development is the aggregation of precipitates due to issues such as errors in fragmentation and misfolding of the $A\beta$ peptide (5, 6).

In this study we aimed to contribute to the definition of the pathogenesis of AD and to reveal potential therapeutic targets, which aimed to reveal the relationship between mitochondrial dysfunction and the pathogenesis of AD and to determine the efficacy of MitoQ, a new generation mitochondrial targeted agent, in $A\beta$ 42-induced SH-SY5Y cells.

Material and Methods

Cell Culture: The human neuroblastoma cell line SH-SY5Y was obtained from American Type Culture Collection. Cells were cultured in Dulbecco's Modified Eagle Medium F-12 (DMEM-F12) supplemented with (10% fetal bovine serum and penicillin/streptomycin) and incubated at 37°C and 5% CO₂.

Preparation of $A\beta$ 42 aggregates: Amyloid beta protein fragment 1-42 ($A\beta$ 42) was purchased commercially (BioLegend, 932502). The $A\beta$ 42 was first dissolved in NH₄OH and then in PBS to 1 mg/ml. The solution was stored at 4°C until use. For aggregation, $A\beta$ 42 solution was prepared to 2 μ M in serum-free DMEM-F12 medium and incubated at 37°C and 5% CO₂ for 3 days.

Establishment of the *in vitro* AD Model: SH-SY5Y cells were treated with 2 μ M $A\beta$ 42 [28] after toxicity assays in the presence and absence of 50 nM MitoQ for 24 hours.

MitoQ Preparation and Treatment: MitoQ (BioVision, B1309) is an orange-brown powder chemical. It was dissolved in DMSO in 50 nM concentration. MitoQ was applied to the $A\beta$ 42 groups for 24 hours.

Cell Viability Assay: Cell viability was assessed by XTT assay (Biological Industries, 20-300-1000). Cells were seeded into 96-well plates and left for adhere for 24h. Then, cells were treated with different concentrations of $A\beta$ 42 for 24 h. Cells in each well were incubated with XTT reagent for 4 h then plates were read by measuring the absorbance at 450 nm and 630 nm with a microplate reader from BioTek epoch®.

Quantitative Real-Time PCR (qRT-PCR): Total RNA was isolated by RNA extraction reagent (GeneAll, 301-001) and reverse transcribed into cDNA with cDNA synthesis kit (BioRad #170-8891). qRT-PCR (Bio-Rad, CFX Connect) was performed by using BrightGreen master mix (ABM, BrightGreen 2X qPCR

MasterMix-ROX, MasterMix-R) with specific primers (Table 1). ACTB was used as internal control and CT values were normalized to ACTB.

Western Blot: Cells from different experimental conditions were lysed with ice-cold RIPA lysis buffer. Cell debris and nuclei were discarded after centrifugation at 14000 rpm for 10 min. The supernatants were collected and protein concentration was measured with Bradford method. 30 µg protein samples were separated by SDS-PAGE. Then, proteins were transferred to PVDF membrane and blocked in 3% skimmed milk. The blots were overnight with primary antibodies Opa1 (STJohn's Laboratory, STJ194724) and β-Actin (Bioss Antibodies, BS-0061R, 1:1000) at 4°C. In the next day, blots were incubated with HRP-conjugated secondary antibody for 2 h at room temperature. Protein bands were visualized using a chemiluminescent enhancer substrate (Elabscience, E-IR-R301). The intensity of the bands was quantified using ImageJ software.

Mitochondrial Membrane Potential Analysis: SH-SY5Y cells were incubated with MitoTracker Red dye (Invitrogen, M7512) for 1 h. After incubation, dye was discarded and DMEM-F12 medium was added. Fluorescent was observed and recorded under fluorescence microscope (ZEISS Axiovert 5).

Intracellular ROS Activity Assay: Intracellular ROS generation was assessed using ROS Fluorometric Assay Kit (Abcam, ab186027). SH-SY5Y cells were incubated with ROS Red Stock Solution for 1h in the incubator. Fluorescent was recorded using a fluorescent plate reader (Ex/Em: 520 nm /605 nm). All values of % ROS level were normalized to the control group.

Statistical Analysis: All data were expressed as mean ± SEM. qRT-PCR data were analyzed with $2^{-\Delta\Delta CT}$ method using RT² Profiler™ PCR Array Data Analysis program. This automated program calculates the fold changes using the given C_T values of the interested genes. The $2^{-\Delta\Delta CT}$ method is a relative quantification approach used in real-time PCR to compare gene expression levels between experimental and control groups. It calculates fold changes by normalizing the C_T values of target genes to a reference gene and then to control sample. Other data were analyzed using GraphPad Prism version 8.0.2. p-value of less than 0.05 was considered statistically significant.

Ethics Committee: Ethics Committee for Non-Pharmaceutical and Non-Medical Device Research Ethics committee approval number: 2018/1563

Ethics committee approval date: November 9, 2018

Informed consent was not required and therefore was not obtained in this study.

Results

The effect of Aβ42 on SH-SY5Y cell viability:

SH-SY5Y cells were treated with 0.1 µM, 0.5 µM, 1 µM, 2 µM and 5 µM doses of Aβ42 for 24 h. According to our results, 0.1 µM, 0.5 µM, 1 µM and 2 µM doses of Aβ42 had no toxic effects on SH-SY5Y cells (Figure 1A). And, 2 µM Aβ42 which caused 5% toxicity was used for further experiments. The morphological features of the cells after Aβ42 exposure were observed under phase-contrast microscope. Aggregates are shown in Figure 1B-C. In the subsequent analysis, cells were treated with 2 µM Aβ42 in the presence and absence of 50 nM MitoQ for 24 hours (7).

Effect of MitoQ on expression level of AD and mitochondrial dysfunction-related genes and Opa1 protein:

We aimed to investigate the effect of Aβ42 and MitoQ on SH-SY5Y cells line in mRNA levels (Figure 2). We found significant differences between Aβ42 and Aβ42+ MitoQ groups comparing to control. The mRNA expressions of *SOD1*, *SOD2* and *CAT* genes was significantly increased Aβ42 + MitoQ group comparing to untreated control and Aβ42. In the terms of BACEs, we found that *BACE1* in Aβ42 + MitoQ groups significantly reduced comparing to untreated control and Aβ42 while *BACE2* significantly boosted in Aβ42 + MitoQ groups. Regarding to Mitochondrial Rho GTPase 1 (*MIRO1*) we found that *MIRO1* significantly increased in Aβ42 + MitoQ comparing to untreated control and AD model. ATPs and COIs are important markers for AD, we found that *ATP6*, *ATP8*, *COI*, *COII* and *COIII* gene expression significantly reduced in Aβ42 + MitoQ groups comparing to AD model and untreated control. In the same manner, we found a significant reduction in Aβ42 + MitoQ groups in terms of *APOE*. Regarding to motor and traffic proteins, we found that *KINESIN I*, *TRAKI*, and *TRAKII* gene expression significantly reduced comparing to just untreated control while *KINESIN I* and *TRAKI* gene expression significantly reduced comparing to untreated control and AD model. β-amyloid precursor protein (APP) is crucial AD marker we found that treating cells AD model cells with MitoQ reduced significantly the gene expression of APP comparing to AD model and control.

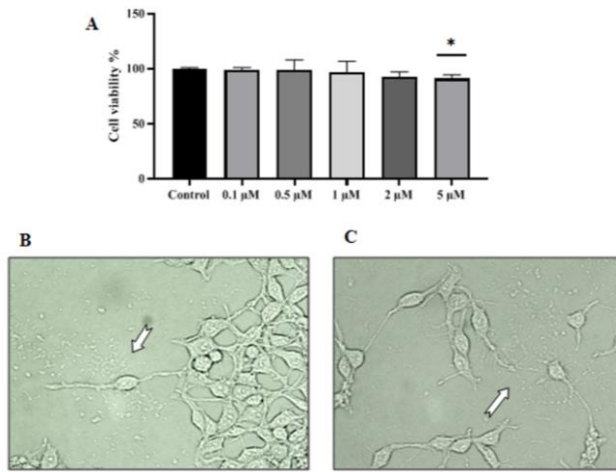


Fig. 1 (A-C) Effect of Aβ42 treatment on SH-SY5Y cells (A). Effect of different concentration of Aβ42 on SH-SY5Y cells after 24h incubation (B). Data were analyzed with GraphPad Prism using multiple T test, $p < 0.05$ (B) Representative images of Aβ42 group SH-SY5Y cells on 2nd day (arrows show Aβ42 aggregates, 630X) (C).

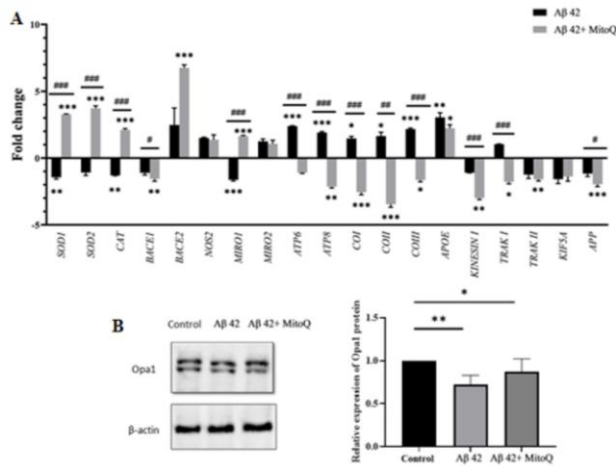


Fig. 2 (A-B) Effect of MitoQ on Alzheimer's models SH-SY5Y cells. (A) Relative transcriptional levels of AD and mitochondrial dysfunction-related genes in Aβ42 and Aβ42+MitoQ treatment groups. (B) Relative Opa-1 protein levels in Aβ42 and Aβ42+MitoQ treatment groups. β-actin used as internal loading control. Data were analyzed with GraphPad Prism using multiple T test, one way ANOVA. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ comparison with the control group; # $p < 0.05$; ## $p < 0.01$; ### $p < 0.001$ comparison between Aβ42 and Aβ42+MitoQ treatment groups

According to western blot results, there is a statistically significant decrease in Opa1 protein expression in Aβ42 group comparing to control group. While in Aβ42+MitoQ group, the protein expression level of Opa1 is similar to that of control group (Figure 3).

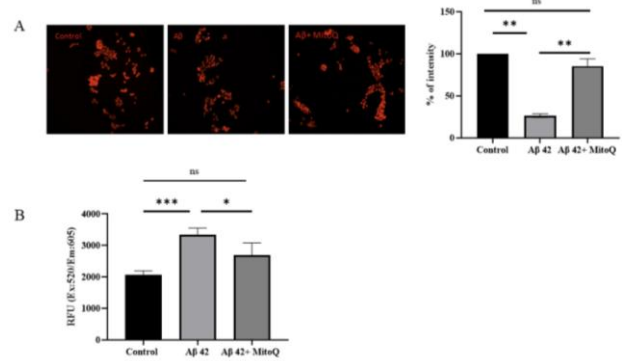


Fig. 3 (A-B) Effect of MitoQ on AD model (A) Mitochondrial membrane potential of Aβ42 and Aβ42 + MitoQ cell groups (Mitochondria are stained with MitoTracker Red fluorescence dye, 200X). (B) Intracellular ROS levels of Aβ42 and Aβ42 + MitoQ cell groups. Data were analyzed with GraphPad Prism one way ANOVA, $p < 0.05$ (*), $p < 0.001$ (**), $p < 0.0001$ (***), and not significant (ns) $p > 0.05$. (RFU: relative fluorescence unit, Ex/Em: excitation/emission wavelengths)

Effect of MitoQ on Mitochondrial Membrane Potential (MMP) and ROS activity in SH-SY5Y cells:

The levels of fluorescent intensity under fluorescent microscope shows MMP (Figure 3A). MMP of cells in Aβ42 group decreased compared to control group while in Aβ42+MitoQ group the MMP is similar to that of control group, increasing compared to Aβ42 group. As regard to intracellular ROS levels, it had been found that ROS levels were decreased significantly in MitoQ treatment comparing to Aβ42 groups and become similar to control (Figure 3B).

Discussion

In neurodegenerative diseases, mitochondrial dysfunction seems to play a key role in the development and progression of neurodegeneration. The prevention of mitochondrial dysfunction is potentially an effective strategy for the treatment of neurodegeneration due to oxidative stress (8). In this study, we investigated the effects of MitoQ against Aβ42-mediated toxicity in SH-SY5Y human neuroblastoma cells by treating them with 2 μM of Aβ42 for 24 h in the presence or absence of 50 nM form MitoQ. We also studied the the effect of MitoQ on mitochondrial membrane potential and antioxidant ability of MitoQ in preventing the Aβ42-induced oxidative stress.

Many genes which play important roles in AD and mitochondrial dysfunction were evaluated.

Table 1: The primer sequences of target genes (SOD1: superoxide dismutase type1, SOD2: superoxide dismutase type2, CAT: catalase, BACE1: beta secretase 1, BACE2: beta secretase 2, NOS2: nitric oxide syntase 2, MFF: mitochondrial fission factor, MIRO1: mitochondrial Rho GTPase 1, MIRO2: mitochondrial Rho GTPase 2, ATP6: ATP synthase membrane subunit 6, ATP8: ATP synthase membrane subunit 8, COI: cytochrome c oxidase I, COII: cytochrome c oxidase subunit 2, COIII: cytochrome c oxidase subunit 3, APOE: apolipoprotein E, KINESIN-1: kinesin-1 heavy chain, TRAK1: trafficking kinesin protein 1, TRAK2: trafficking kinesin protein 2, KIF5A: kinesin family member 5A, APP: amyloid-beta precursor protein)

| NO | Gene Name | Forward Primer (Sense) | Reverse Primer (Antisense) |
|----|-----------|--------------------------|----------------------------|
| 1 | SOD1 | GATGAAGAGAGGCATGTTGGAG | CTCCTGAGAGTGAGATCACAGA |
| 2 | SOD2 | GGAGATGTTACAGCCCAGATAG | CGTTAGGGGCTGAGGTTTGT |
| 3 | CAT | AGGGTGGTGCTCCAAATTAC | TGTTGAATCTCCGCACTTCTC |
| 4 | BACE1 | ATCCACGGGCACTGTTATG | GTCATGAGGGTTGACTCATCTG |
| 5 | BACE2 | CACAGAGAGGTCTAGCACATAC | GGCCAAGTATTCATTCATTT |
| 6 | NOS2 | GTTTCGGGAAGTGGAGCTAAA | CCCATGTACCAGCCATTGAA |
| 7 | MFF | AACCTCTGGGAAGAGGAGAACAAA | CGAAACCAGAGCCAGCTATTA |
| 8 | MIRO1 | GTGGACGCTCACGACTTATT | AGCTGAAGCTTGAGACTCTTG |
| 9 | MIRO2 | TTGATGGCAGTGACCCAAA | GCCTTGGAGGAGACAAAGAG |
| 10 | ATP6 | CCACCTACTCATGCACCTAAT | AGCGATTTCTAGGATAGTCAGTAG |
| 11 | ATP8 | CTACCACCTACCTCCCTCAC | GGGCAATGAATGAAGCGAAC |
| 12 | COI | CTAGCAGGTGTCTCCTCTATCT | GGCGTTTGGTATTGGGTTATG |
| 13 | COII | ATCCCTCCCTTACCATCAAATC | GTCGCCTGGTTCTAGGAATAAT |
| 14 | COIII | CGAGTCTCCCTTACCATTTC | TTGGCGGATGAAGCAGATAG |
| 15 | APOE | CGTTGCTGGTCACATTCCT | CCTTCAACTCCTTCATGGTCTC |
| 16 | KINESIN-1 | CAGCAAAGTCAACTGGTAGAGA | GCTCAGCTTGCATATTGTCTTG |
| 17 | TRAK1 | CCGACACCATCTACGGTATATG | GTCTCTTCAATTTGCTCGGTIG |
| 18 | TRAK2 | CAACCGACGAGATTCCACTAC | AATTGGGCTGTGGTACACTT |
| 19 | KIF5A | GAGAAGCTGAAGAGCGAAGAA | CTCATGTCGCTCGTACAGAAA |
| 20 | APP | GACAGACAGCACACCCTAAA | GGCCAAGACGTCATCTGAATA |

Superoxide dismutases (SODs) are a crucial antioxidant defense against oxidative stress in the body. The enzyme is effective in treating illnesses caused by reactive oxygen species (9). In our study, it has been found that Superoxide dismutase 1 (*SOD1*), Superoxide dismutase 2 (*SOD2*) and Catalase (*CAT*) reduced in AD model while applying the MitoQ increased their expression. It is familiar that decreasing SODs activity in AD models (10, 11). In primary culture of mice neuron cells, the effect of MitoTEMPO, which is another mitochondria-targeted antioxidant molecule, was searched. A β 42 or MitoTEMPO showed no significant difference on *SOD2* expression (12). Turkseven and his peers (2019) showed that MitoQ increased the expression of MnSOD, Cu/ZnSOD and catalase expressions getting into their levels of control group in liver inflammation in rats. A β 42 peptide

decreased the SOD enzyme protein expression level in SH-SY5Y neuroblastoma cells (13).

BACE1 gene encodes the beta secretase enzyme which is responsible for the production of A β 42 peptide in neurons. *BACE1*-knockout mice were shown to lack A β 42 production and Alzheimer related pathologies such as neuron and memory loss (14). *BACE1* is also an important gene playing role in myelin sheath. Its expression level was found to be high during myelination process in postnatal period of mice (15). In our study it has been found that *BACE1* expression decrease in A β 42+MitoQ group compared to A β 42 group ($p < 0.05$). The decrease of *BACE1* expression after MitoQ application may back to the inhibitory effect of MitoQ on A β 42 production. Mitochondrial Rho-GTPase 1 (Miro1), a protein located on the outer mitochondrial membrane, has been identified as a key regulator of mitochondrial transport. This process is vital for ensuring the

protection of neurons (16). In our study we found that MitoQ increase *Miro1* gene expression comparing to control and to AD model. Actually, *Miro1* has a neuroprotectivity affect. In the terms of ATPs and Cytochrome c oxidase subunit (Cos), we have found that *ATP6*, *ATP8*, *COI*, *COII* and *COIII* significantly increased in AD model while decreased in MitoQ, which is agreed with a lot of studies like (17). With regard to apolipoprotein E (APOE) we found that MitoQ decreased *APOE* significantly comparing to the control and AD model. Actually, *APOE* decreases reduce AD risk and helps lifespan as mention in (18). As regards KINESIN I which is a motor protein that transports cargo along microtubules (19). This protein increases in AD models due to the adaptive response to impaired axonal transport (20). We found that MitoQ reduce this gene expression significantly under the control. The trafficking kinesin protein (TRAK) protein family consists of kinesin adaptors that have been linked to neuronal mitochondrial trafficking via their interactions with the mitochondrial protein Miro and kinesin motors (21). These proteins linked to degenerative diseases (22). As expected *TRAKI* and *TRAKII* were decreased in MitoQ treatment. In Alzheimer's disease, β -amyloid precursor protein (APP) is cleaved to create $A\beta$, which collects in the brain. Changes in the APP gene sequence or expression may have an impact on $A\beta$ levels and illness risk (23). In our study we have found that MitoQ significantly decreased *APP* gene comparing to control.

The Opa1 protein is involved in a variety of functions, including the maintenance of respiratory chain and membrane potential, the organisation of cristae, and the regulation of apoptosis and the maintenance of mitochondrial DNA. Nonetheless, all studies concur that Opa1 on the mitochondrial inner membrane, along with MFN1 and MFN2 on the outer membrane, is required for mitochondrial fusion and that this process is controlled by proteolytic cleavage of Opa1 (24). *OPA1* gene and protein expression related to mitochondrial dysfunction and Alzheimer's (25). On the other hand, Mitochondrial fission factor (Mff) is a membrane protein that controls mitochondrial fragmentation and recruits Drp1 to the fission area (26). It has been found that *MFF* upregulated in AD (27) and so we investigated Opa1 protein expression levels. We have found that *OPA1* protein expression decreased $A\beta$ 42 while increased $A\beta$ 42+MitoQ group comparing to control. Ahmed, et al. (2019) investigated the effect of $A\beta$ 42 oxidative stress-

related glia maturation factor proteins on the expression of mitochondrial fission and fusion proteins (28). They found that $A\beta$ 42 decreased the expression of fusion proteins including Opa1 protein. In our study, we've also found that $A\beta$ 42 decreased Opa1 protein expression, which infers the ability of $A\beta$ 42 peptide to cause mitochondrial dysfunction in our cell model.

Literature shows that there is decrease of MMP in AD. MitoTracker Red fluorescence intensity showed the MMP change between the groups. In $A\beta$ 42 group, there was a decrease in MMP while there was an increase in $A\beta$ 42+MitoQ group. 7PA2 and 7WD4 cells produce $A\beta$ 42 peptide continuously so they are suitable for studying the $A\beta$ 42 toxicity. Krako, et al (2013) showed that the MMP in 7PA2 and 7WD4 cells were less than control cells (29). MitoTEMPO molecule increased the MMP after it was decreased because of $A\beta$ 42 exposure (12). These results show that $A\beta$ 42 causes oxidative stress-related mitochondrial dysfunction And MitoQ returns this effect. On the other hand, ROS levels were increased in 40% in $A\beta$ 42 group compared to control and decreased in $A\beta$ 42+MitoQ group compared to $A\beta$ 42 group. ROS production was decreased by MitoQ in platelets (30). ROS levels in 7PA2 and 7WD4 cells were higher than the control cells (29). Thus, $A\beta$ 42 causes oxidative stress and MitoQ molecule decreases the ROS production.

In muscle-specific $A\beta$ 42 expressing AD model transgenic *C. elegans*, MitoQ affected life-span and quality in a positive manner even if it did not decrease ROS level and mtDNA damage (31). The protective effect of MitoQ against $A\beta$ 42 toxicity was shown in primary neuron culture. In triple-transgenic mouse model, MitoQ decreased the AD-like neuropathology. MitoQ decreased oxidative stress, $A\beta$ 42 accumulation, astrogliosis, synaptic loss and caspase activation in mice brain tissues (32). Solesio et al. (2013) showed the neuroprotective effect of MitoQ on Parkinson's disease cell and mouse models (7). The cardioprotective effect of MitoQ was also investigated and they revealed the decrease of the cardiac hypertrophy, oxidative and mitochondrial damage (33, 34).

Our study showed that the statistically significant decrease in protein expression levels observed in the $A\beta$ +MitoQ group compared to the $A\beta$ group may indicate that MitoQ brings the mitochondrial fission process closer to physiological levels. $A\beta$ is associated with the induction of oxidative stress, and due to the mitochondria-targeted antioxidant

properties of MitoQ, intracellular ROS production is significantly decreased.

We successfully created an Alzheimer's model utilizing A β 2 and studied the effect of the mitochondria-targeted antioxidant molecule, MitoQ, on oxidative stress and mitochondrial dysfunction in this work. We discovered substantial changes in gene and protein expression, as well as changes in mitochondrial membrane structure. These findings, together with MitoQ's possible therapeutic benefits, indicate the drug's potential as a treatment for Alzheimer's disease. Performing dose-dependent and time-dependent experiments for A β and MitoQ may provide more definitive results. Furthermore, the study was conducted using a single cell line. Thus, 3D cell culture systems and animal investigations are needed to corroborate these findings and get more accurate insights, especially in organs immediately impacted, such as the brain.

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