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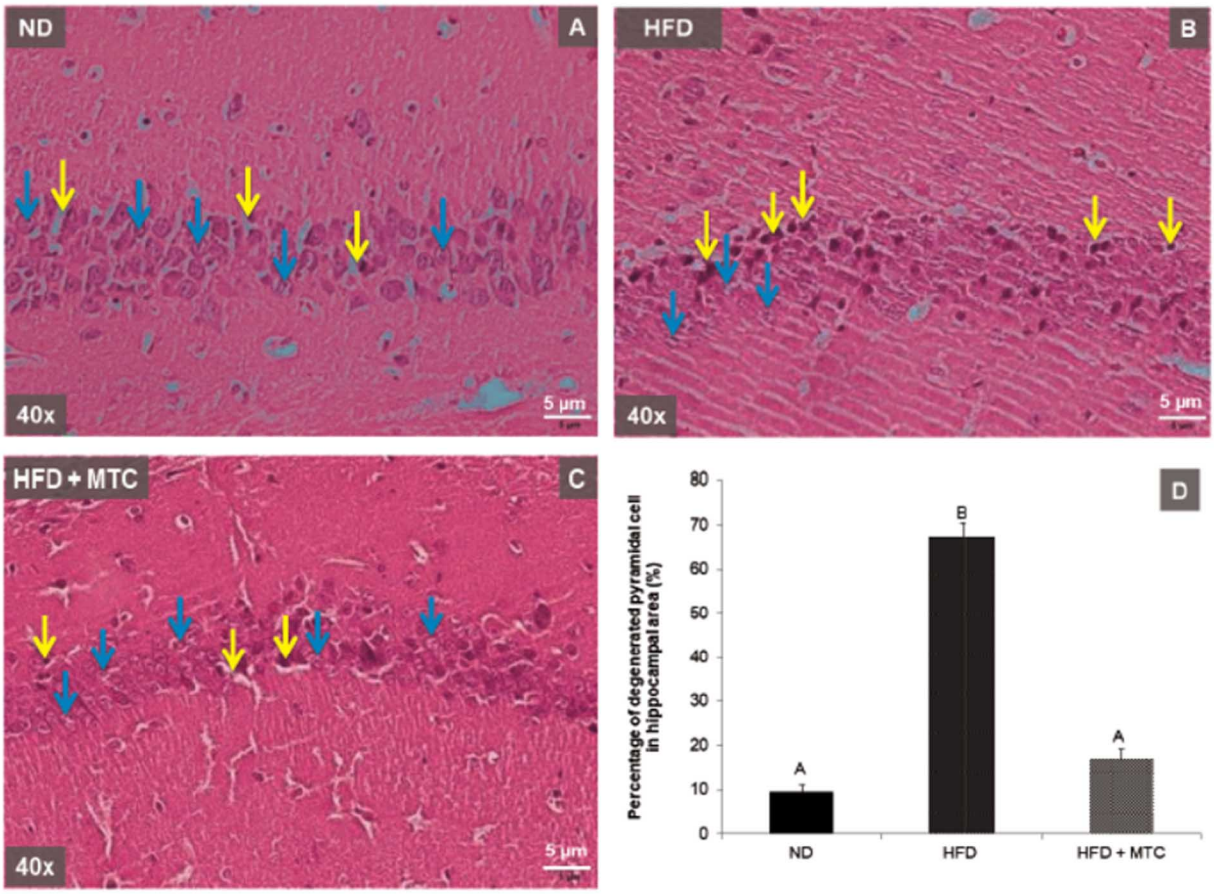

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AIM AND SCOPES
Journal of Cellular Neuroscience and Oxidative Stress is an online journal that publishes original research articles, reviews and short reviews on the molecular basis of biophysical, physiological and pharmacological processes that regulate cellular function, and the control or alteration of these processes by the action of receptors, neurotransmitters, second messengers, cation, anions, drugs or disease.

Areas of particular interest are four topics. They are;

A- Ion Channels (Na^+- K^+ Channels, Cl^- channels, Ca^{2+} channels, ADP-Ribose and metabolism of NAD^+, Patch-Clamp applications)

B- Oxidative Stress (Antioxidant vitamins, antioxidant enzymes, metabolism of nitric oxide, oxidative stress, biophysics, biochemistry and physiology of free oxygen radicals)

C- Interaction Between Oxidative Stress and Ion Channels in Neuroscience
(Effects of the oxidative stress on the activation of the voltage sensitive cation channels, effect of ADP-Ribose and NAD^+ on activation of the cation channels which are sensitive to voltage, effect of the oxidative stress on activation of the TRP channels in neurodegenerative diseases such Parkinson's and Alzheimer's diseases)

D- Gene and Oxidative Stress
(Gene abnormalities. Interaction between gene and free radicals. Gene anomalies and iron. Role of radiation and cancer on gene polymorphism)

READERSHIP

Biophysics	Biochemistry
Biology	Biomedical Engineering
Pharmacology	PhysiologyGenetics
Cardiology	Neurology
Oncology	Psychiatry
Neuroscience	Neuropharmacology

Keywords
Ion channels, cell biochemistry, biophysics, calcium signaling, cellular function, cellular physiology, metabolism, apoptosis, lipid peroxidation, nitric oxide, ageing, antioxidants, neuropathy, traumatic brain injury, pain, spinal cord injury, Alzheimer's Disease, Parkinson's Disease.

RESEARCH ARTICLE

J Cell Neurosci Oxid Stress 2024;16(1): 1173-1182

Neuroprotective Effect of *Colocasia esculenta* Var. Mentawai Corm Flour on Oxidative Stress in Mice Fed a High-Fat Diet

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List of Abbreviations;

***CNS,** Central Nervous System; **DDY,** Deutschland Denken Yoken; **GC-MS**, Gas Chromatography-Mass Spectrometry; **HFD**, High Fat Diet; **MDA,** Malondialdehyde; **MTC,** Mentawai Taro Corm; **Nrf2**,* nuclear factor erythroid 2-related factor 2; ***SCFA,** Short Chain Fatty Acid.*

Abstract

The shift in dietary habits towards greater consumption of fatty foods, brought about by the transformation of our period, poses a global health concern. Neurodegeneration, which results in cognitive impairment, is one of these difficulties. To overcome the drawbacks of non-natural therapy modalities, it is essential to look for natural alternatives. One such alternative is utilizing the properties of secondary metabolite compounds found in plants, such as *Colocasia esculenta* Var. Mentawai. This research aims to assess the efficacy of *C. esculenta* Var. Mentawai corm as a neuroprotective agent in mitigating Central Nervous System (CNS) damage and preventing cognitive decline associated with neurodegeneration. For sixty days, young adult male mice are given a high-fat diet and a taro flour mixture on a daily basis. Additionally, the neurocognitive abilities of the mice were analyzed, the amounts of malondialdehyde (MDA) were measured, and the histological structures of brain tissue were observed. The results showed that the group of mice fed with the taro flour mixture effectively exhibited a positive impact on maintaining neurocognitive abilities and histopathological structure of brain tissue against neurodegeneration. However, there was no significant effect on the suppression of MDA levels in the brain when comparing treatment groups. It has been found that Mentawai taro flour is effective in preserving the brain against neurodegenerative events by preventing nerve degeneration in the hippocampal area and cerebral cortex. Consequently, Mentawai taro flour emerges as a robust candidate for functional food with the potential to address global health issues associated with neurodegeneration.

Keywords; High-fat diet, Mentawai taro flour, neurodegeneration, obesity, secondary metabolites.

Introduction

Neurodegenerative diseases involve a series of pathological changes that cause nerve damage, resulting in a progressive decline in cognitive function. Various factors can trigger neurodegeneration, with one significant contributor being the shift towards an unhealthy diet characterized by the consumption of fast food rich in high fat. High fat intake has been associated with damage to the central nervous system, manifesting in neuropsychiatric disorders such as dementia and Alzheimer's disease (Morys et al., 2023). Health problems stemming from the consumption of high-fat foods are a serious global problem and are expected to continue to increase.

Diverse studies and research endeavors are crucial for addressing the pressing issue of neurodegeneration. The current provision of drugs for preventing and treating this condition is not without drawbacks, as they often contain non-natural ingredients and can lead to various side effects. Moreover, these medications can be relatively expensive for certain individuals. (Kennedy et al., 2018). Hence, a solution-oriented approach is imperative in addressing physiological diseases resulting from high-fat diet consumption. This involves utilizing natural components found in plants, which may hold the potential for mitigating neurodegenerative events due to the antioxidant content inherent in these plants. Plants contain flavonoids in large quantities as the main antioxidant defense that can act as an anticancer, neuroprotective, antidiabetic, anti-inflammatory, and free radical exterminator (Chen et al., 2019). The role of flavonoids in plants has been proven in a growing number of studies. Flavonoids can prevent cell damage in the body caused by various physiological disturbances. Through the mechanism of decomposing free radicals, flavonoids can increase endogenous antioxidant enzyme levels and reduce malondialdehyde (MDA) levels, which are indicators of oxidative stress (Yildizhan et al., 2020). Additionally, compounds in the flavonoid group, such as hesperidin, have shown potential in preventing cell damage by reducing TRPM2 channel activity, type-4 collagen, and fibrinogen immunoactivity (Bayir et al., 2023).

One plant that contains antioxidant compounds is corms such as Mentawai taro (*Colocasia esculenta* (L.) Schott). *C. esculenta* (L.) Schott is a corm plant naturally found in the Mentawai Islands, Indonesia. The people of the Mentawai Islands commonly use Mentawai taro as a staple food, alongside sago. Additionally, *C. esculenta* (L.) contains secondary metabolite compounds that act as antioxidants and anti-inflammatory agents (Rustiani et al., 2021). Taro corm also boasts a high fiber content, leading to the formation of short-chain fatty acid (SCFA) that serve as anti-inflammatory agents, thus aiding in preventing physiological damage (Galisteo et al., 2008). Thus, Mentawai taro holds potential as a neuroprotector against neurodegenerative diseases resulting from the consumption of a high-fat diet. Notably, there have been no reports on studies discussing the potential of Mentawai taro corm in combating neurodegeneration. Therefore, this research aims to ascertain the neuroprotective benefits of Mentawai taro corm flour in a mice model, providing an alternative solution to global challenges related to food consumption by maintaining neurocognitive abilities by protecting histopathological structure and decreasing the production of MDA in the brain.

Materials and Methods

Material Collection and Authentication

Mentawai Taro corms *C. esculenta* (L.) Schott were sourced from Sipora Village, Mentawai Islands Regency, West Sumatra, Indonesia, and their species identities were confirmed by certified botanists at the ANDA Herbarium, Andalas University.

Preparation of Mentawai Taro Flour

Taro flour was obtained by drying mashed taro tubers' wet preparation using an automatic steamer (PHILIPS HD-9104, Netherlands) at 70°C for 19 hours in an oven (Emmert UN55, Germany). The dried taro was then ground and pulverized into powder using an electric grinder (TENCAN Model XQM-0.4 A, China). The preparation process of taro flour adhered to the procedures outlined in a previous research by Santoso and Maliza (2020).

Animal Models and Experimental Design

Twenty-five young male white mice (DDY strain, 2 months old, ±18-34 g BW) were procured from the Veterinary Monitoring and Investigation Center in Baso, Bukittinggi, West Sumatra, Indonesia. Prior to the experiment, all mice underwent a one-week acclimatization period in an animal conditioning room. They were housed in a room with a 12-hour light/dark cycle, provided with chow (Rat Bio, PT Citra Ina Feedmill, Jakarta, Indonesia), and had access to tap water ad libitum.

All procedures involving the animals were approved by the Research Ethics Committee, Faculty of Medicine, Andalas University (Approval No. 528/UN.16.2/ KEP-FK/2021). Following the acclimatization phase, the mice were randomly divided into three groups, with five mice per group as follows:

Group 1 (ND): Normal Diet
Group 2 (HFD): High Fat Diet (HFD)
Group 3 (HFD + MTC): HFD (21%) + Mentawai Taro Corm (MTC) (25%)

The daily experimental feed given to mice over an 8-week period consisted of 210 g of butter and 250 g of taro flour. The composition of the feed mixture was determined based on findings from previous research (Yang et al., 2012).

Hebb William Maze Test

The memory intelligence test was conducted using the Hebb William Maze. The test animals underwent three days of training prior to testing, with each training session lasting one hour per day. The parameter observed was the time required by the test animals to complete the maze. Testing was carried out in the afternoon at 4:30 p.m. when the animals were most active. The test followed a protocol based on previous research (Boutet et al., 2018).

Hole Board Test

The curiosity test was conducted using a cube-shaped device measuring 40 x 40 cm equipped with a perforated board containing 16 holes arranged in the same pattern. The parameter measured during the test was the frequency of head dipping by the test animal into the holes within a 5-minute period. This test followed a protocol established in previous research (Havas et al., 2011).

Measurement of Malondialdehyde (MDA) Levels

After being fed the experimental diet for 8 weeks, mice were sacrificed, and brain samples were collected. MDA levels in brain tissue homogenates were determined using the thiobarbituric acid method. The samples were incubated for 30 minutes at 100°C. After cooling, the samples were centrifuged at 1,500 rpm (Thermo Fisher Scientific) for 10 minutes, and the supernatant was collected. The resulting supernatant was then analyzed for absorbance value at λ 530 nm using a spectrophotometer (UV-Vis Biorad), and the filtrate was separated. The analytical method has been described in a previous study (Darvishi-Khezri et al., 2017).

Histopathological Examination of Brain

After dissection, rat brain samples were immediately preserved in 10% formaldehyde (Sigma-Aldrich, Merck Darmstadt, Germany). Subsequently, the samples underwent tissue processing following standard protocols, as previously described by Isaac et al. (2023) and Jordan et al. (2011). Specimens were stained with hematoxylin-eosin stain (TissuePro Technology EY07-500R, h08-500r, Gainesville, FL), and an examination of histopathological changes in brain tissue, particularly in the hippocampus and cerebral cortex, was performed using a light microscope (Olympus CX43, Olympus, Tokyo, Japan). The thickness of the cerebral cortex layer and the number of degenerated pyramidal cells in the hippocampus and cerebral cortex were observed at 10x and 40x magnifications across 5 fields of view. The thickness of the cerebral cortex layer was measured by drawing perpendicular lines from the cortex surface to the grey matter boundary at 10 different points and then averaged. Meanwhile, the percentage of cell damage was determined by counting the surviving and degenerated cells in both the cerebral cortex layer and hippocampal area. The results of the histopathological structure observations were analyzed using ImageJ software (ImageJ 1.49v, NIH, USA) following the method outlined by Simon et al. (2013) for observing histopathological changes in brain tissue.

Statistical Analyses

All results are expressed as mean ± standard deviation (SD) and p values less than $p \leq 0.05$ were considered significant. To determine the effect of treatment, data were analysed using one-way ANOVA. Post-hoc tests were used on all data that had statistically significant differences. The existence of significance was assessed by Duncan's multiple range test with SPSS version 25 (IBM Corporation, USA).

Results

Effect of Mentawai taro flour *Colocasia esculenta* (L.) Schott on neurocognitive ability

Hebb William Maze was used to test the spatial working memory, learning ability, and road recall in mice through the maze pathway. Based on **Fig 1**, there was a significant difference in memory ability between mice fed with taro flour and those that were not. This indicates that the maintenance of neural conditions related to memory ability in mice is influenced by the properties of Mentawai taro flour.

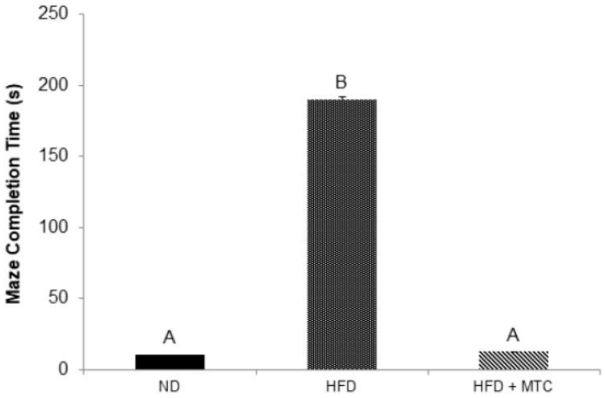

Figure 1. *Effect of Mentawai taro corm (MTC) flour on Hebb William Maze completion time of HFD-fed mice. ND (Normal Diet) (n=5; 10,422 ± 0,43 second), HFD (Normal Diet + butter 21%)(n=5; 190,026 ± 4,17 second), and HFD + MTC (25%)(n=5; 12,446 ± 0,87 second). Different uppercase letters in the diagram indicate significant differences (p<0.05). HFD= High Fat Diet.*

In addition, in **Fig 2**, there is also a significant difference between the group of mice that consumed taro flour and those that did not regarding curiosity in Hole Board testing. This is shown by the frequency of Head Dipping of mice consuming taro flour approaching the control group. This condition can provide information that there is a given effect of taro flour on the maintenance of neurocognitive abilities in the test animals.

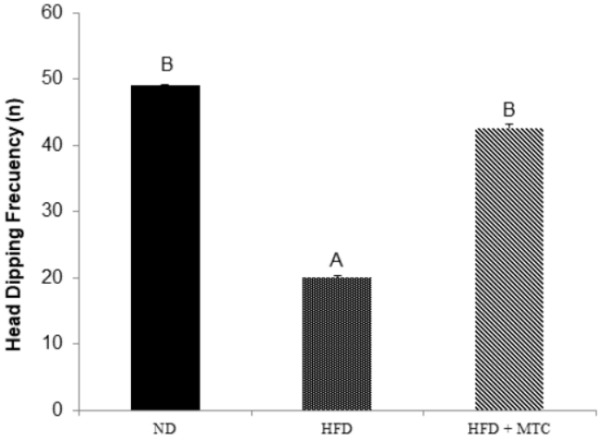

Figure 2. *Effect of Mentawai taro corm (MTC) flour on dipping frequency of mice based on hole board test. ND (Normal Diet) (n=5; 49 ± 0,24), HFD (Normal Diet + butter 21%)(n=5; 20 ± 0,84), and HFD + MTC (25%)(n=5; 42,6 ± 1,24). Different uppercase letters in the diagram indicate significant differences (p<0.05). HFD= High Fat Diet.*

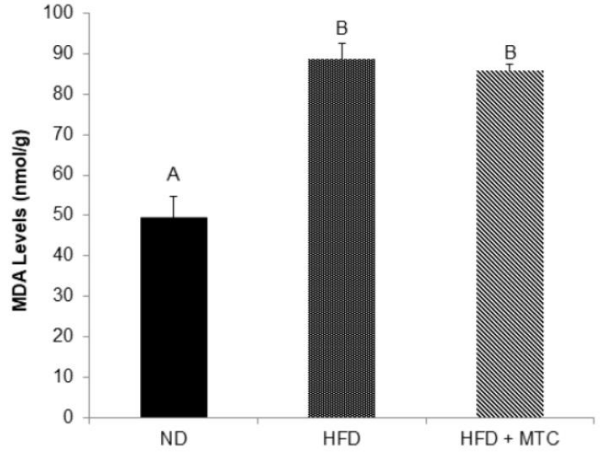

Figure 3. *Effect of Mentawai taro corm (MTC) flour on MDA levels in the brains of mice. ND (Normal Diet)(n=3; 49,1 ± 9,68 nmol/g of tissue), HFD (Normal Diet + butter 21%)(n=3; 88,5 ± 7,06 nmol/g of tissue), and HFD + MTC (25%)(n=3; 85,83 ± 2,68 nmol/g of tissue). Different uppercase letters in the diagram indicate significant differences (p<0.05). HFD= High Fat Diet.*

Effect of Mentawai taro flour *Colocasia esculenta* (L.) Schott on brain MDA concentration

As shown in **Fig 3**, there are no significant differences in the levels of MDA in brain tissue. However, the presence of a secondary metabolite in plants, such as astaxanthin found in Mentawai taro corm (Santoso, 2022) should be able to prevent an increase in MDA levels in the brain. The insignificant difference in the level of MDA

between the treatments using Mentawai taro corm may be due to the short duration of the research, which has not yet yielded a major effect on physiological conditions, as could be possible through mechanisms that support endogenous antioxidant activity in the body. This is demonstrated by the different histopathological structural changes observed between treatments, as shown in **Fig 4, 5,** and **6.**

The cerebral cortex layer in the high-fat diet treatment group without taro flour experienced significant thinning compared to the control. Conversely, MTC (HFD + MTC 25%) maintained the thickness of the cerebral cortex layer, preventing thinning. Pyramidal cells in the cerebral cortex region were markedly reduced in the HFD group but maintained in the MTC group (**Table 1**)(**Fig 5**).

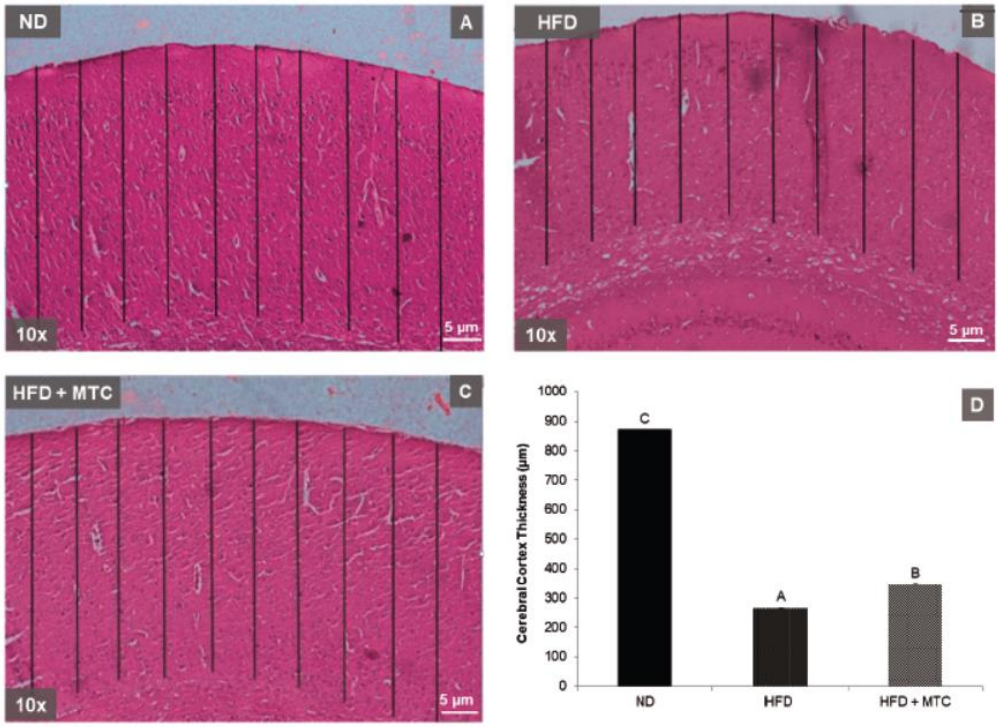

Figure 4*. Effect of Mentawai taro corm (MTC) flour on the cerebral cortex thickness of mice (magnification 10x; A, B, C, Olympus CX43). ND (Normal Diet) (n=5; 870,266 ± 0,56 µm), HFD (Normal Diet + butter 21%)(n=5; 266,554 ± 0,72 µm), and HFD + MTC (25%)(n=5; 345,046 ± 1,62 µm). Different uppercase letters in the diagram indicate significant differences (p<0.05). A= Normal Diet; B= High Fat Diet (HFD); C= (HFD + MTC); D= Graphic of the average thickness of the layers of the cerebral cortex. Scale bars 5 µm.*

Effect of Mentawai taro flour *Colocasia esculenta* (L.) Schott on the histopathological structure of the brain

Histological observations in the brain focused on the thickness of the layers of the cerebral cortex and the number of pyramidal cells in the hippocampus and cerebral cortex, as depicted in **Fig 4**.

In the hippocampal region, the number of pyramidal cells in the HFD group also decreased significantly compared to the MTC group, which maintained the number of pyramidal cells close to the control. The highest proportion of pyramidal cell damage obtain ed in the HFD group showed a statistically significant difference compared to the MTC group (**Table 2**)(**Fig 6**).

Table 1. Percentage of degenerated cells in cerebral cortex

Group	n	Percentage of degenerated pyramidal cells in cerebral cortex (%) ± SD
ND (normal diet)	5	11,27 ± 3,98[a]
HFD (high-fat diet)	5	69,17 ± 6,88[b]
HFD + MTC (mentawai taro corm)	5	20,14 ± 8,79[a]

Note: Numbers followed by different lowercase letters in the same column indicate significant differences in Duncan's post hoc test (p<0.05).

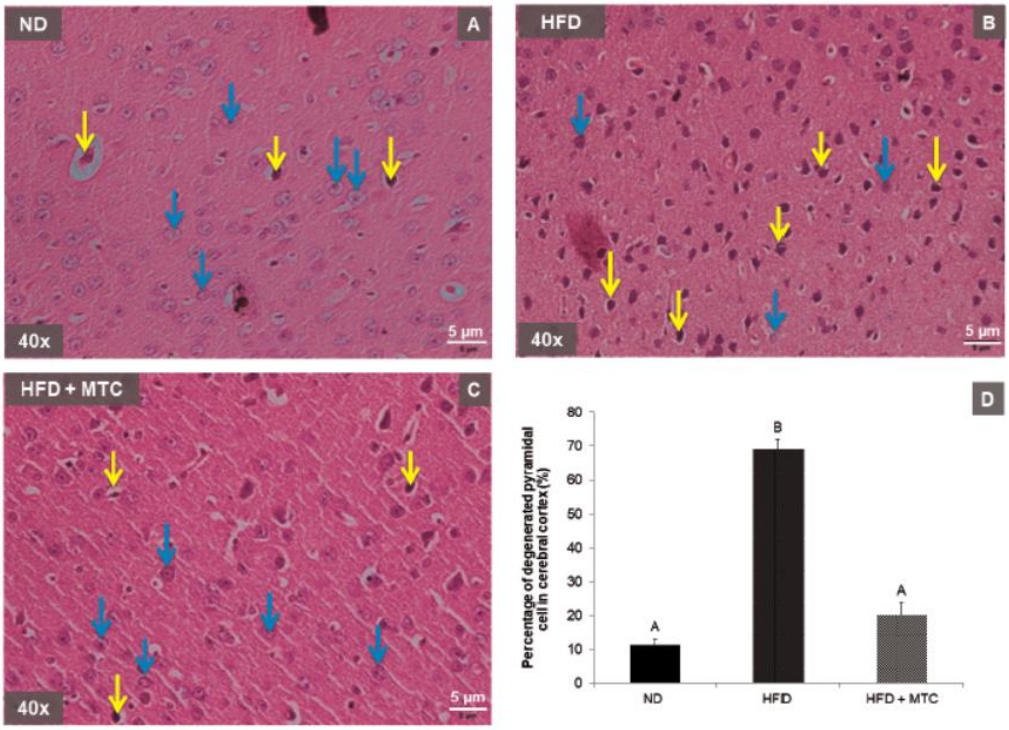

Figure 5. *Effect of Mentawai taro corm (MTC) flour on the number of pyramidal cells in the cerebral cortex of mice (magnification 40x; A, B, C, Olympus CX43). ND (Normal Diet)(n=5; 11,27% ± 3,98), HFD (Normal Diet + butter 21%)(n=5; 69,17% ± 6,88), and HFD + MTC (25%)(n=5; 20,14% ± 8,79). Different uppercase letters in the diagram indicate significant differences (p<0.05). A= Normal Diet; B= High Fat Diet (HFD); C= (HFD + MTC); D= Graphic percentage of the degeneration cells in the cortex cerebral. Blue arrow= cell viable; yellow arrow= cell degeneration. Scale bars 5 µm.*

Discussion

This research demonstrates the neuroprotective effect of Mentawai taro flour against cognitive impairment and neurodegeneration in mice fed a high-fat diet. The administration of taro flour proves effective in preventing nerve degeneration related to memory, particularly in the cerebral cortex and hippocampus. This research highlights the potential of supporting endogenous antioxidant activity through taro flour, as evidenced by the preservation of brain tissue from neurodegeneration. The production of MDA in the brain signifies cell damage induced by free radicals, particularly in the HFD group. Consumption of a high-fat diet can diminish antioxidant activity, leading to an upsurge in the production of inflammatory compounds or molecules such as adipokines and interleukin-6 (IL-6) across various parts of the brain, thereby facilitating lipid peroxidation.

Consuming fiber-rich foods, such as corms, can have a positive effect on addressing the issue of lipid peroxidation. This effect is attributed to the production of SCFA and the presence of secondary metabolite compounds, which play a role in preventing oxidative stress leading to neurodegeneration. These antioxidant compounds can activate the Nrf2 pathway, inhibiting the accumulation of inflammatory molecules and increasing the production of antioxidant compounds as an endogenous defense, as demonstrated in previous research, and protect the brain structure from damage (Abdel Razek et al., 2023; Gonzales-Bosch et al., 2021). The protective effect on nerve cells in the brain from antioxidant activity has a positive impact on memory and cognitive intelligence in the central nervous system.

Table 2. Percentage of degenerated cells in hippocampal area

Group	n	Percentage of degenerated pyramidal cells in hippocampal area (%) ± SD
ND (normal diet)	5	9,50 ± 3,19[a]
HFD (high-fat diet)	5	67,22 ± 7,22[b]
HFD + MTC (mentawai taro corm)	5	17,00 ± 4,74[a]

Note: Numbers followed by different lowercase letters in the same column indicate significant differences in Duncan's post hoc test (p<0.05).

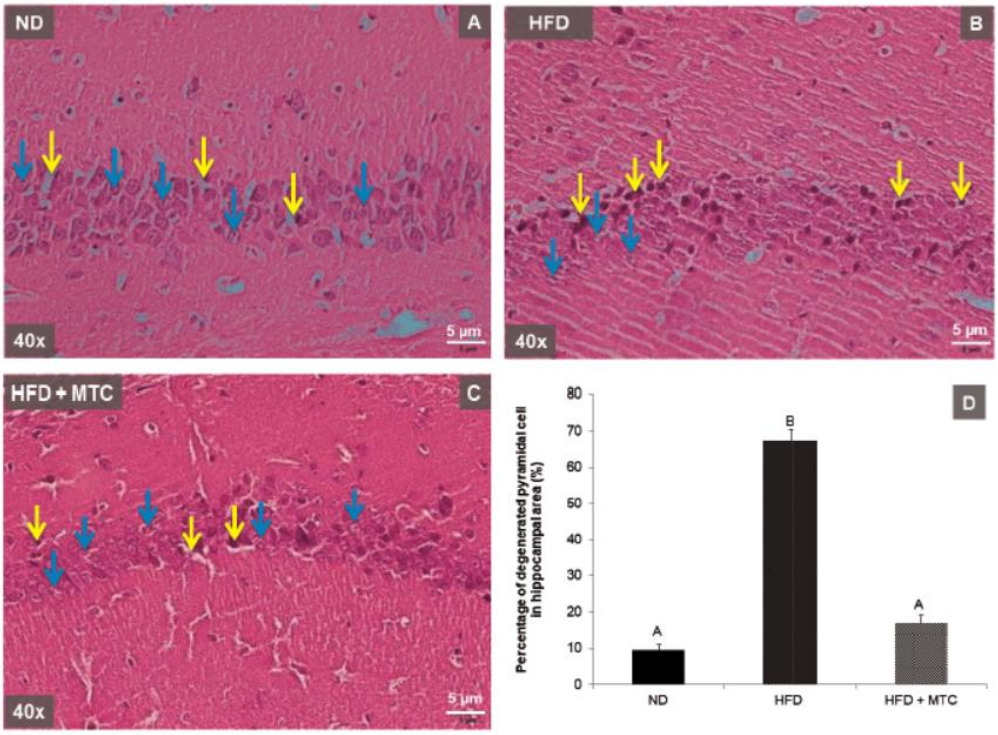

***Figure 6**. Effect of Mentawai taro corm (MTC) flour on the number of pyramidal cells in the hippocampal area of mice (magnification 40x; A, B, C, Olympus CX43). ND (Normal Diet)(n=5; 9,50% ± 3,19), HFD (Normal Diet + butter 21%)(n=5; 67,22% ± 7,22), and HFD + MTC (25%)(n=5; 17,00% ± 4,74). Different uppercase letters in the diagram indicate significant differences (p<0.05). A= Normal Diet; B= High Fat Diet (HFD); C= (HFD + MTC); D= Graphic percentage of the degeneration cells in the hippocampal area. Blue arrow= cell viable; yellow arrow= cell degeneration. Scale bars 5 µm.*

Consumption of taro flour also exerts a protective effect against neurodegeneration of brain tissue, preventing thinning of the cerebral cortex layer. Thinning of the cerebral cortex layer in HFD mice occurs due to apoptosis and cell necrosis induced by oxidative stress from lipid peroxidation. Previous research has reported that the consumption of a high-fat diet can lead to mitochondrial dysfunction, resulting in cell necrosis and apoptosis (Moraes et al., 2009). This event also impacts the histopathological structure of the brain, particularly related to memory, manifesting as the thinning of the layers of the cerebral cortex due to a decrease in the number of viable cells (Gómez-Apo et al., 2021).

The preservation of the thickness of the cerebral cortex layer due to the consumption of taro flour is influenced by the production of SCFA and the content of taro metabolite compounds, enhancing the performance of the Nrf2/HO-1 pathway and inhibiting the Bcl-2/Bax pathway, which in turn prevents cell necrosis triggered by mitochondrial dysfunction due to oxidative stress. Another histopathological structure of brain tissue influenced by oxidative stress is the number of pyramidal cells in the hippocampus and cerebral cortex areas. The consequences of consuming a high-fat diet, which is linked to mitochondrial dysfunction leading to cell necrosis, can be mitigated by responding to increased compound production and the activation of antioxidant genes. These responses are triggered by an enhanced performance of the Nrf2/HO-1 pathway (Fock and Parnova, 2023; Gong et al., 2014).

If linked to previous research the results of this study indicate that consuming taro flour can protect nerve cells from degeneration due to high-fat consumption. This supports our hypothesis that taro flour is beneficial in preventing cognitive dysfunction and damage to the histopathological structure of brain tissue caused by various physiological disorders leading to nerve damage and/or degeneration and decreased neurocognitive abilities. Taro flour influences the production of SCFA through the fermentation of indigestible carbohydrates. In addition, it also contains secondary metabolite compounds that act as antioxidants and anti-inflammatories as shown in **Table 3.**

Previous research has also identified specific phytochemicals in Mentawai taro corm that act as antioxidants and anti-inflammatories at the cellular level as shown in **Table 4.**

Table 3. Content of secondary metabolite compounds in *C. esculenta* corm (Ouedrago et al., 2023).

No	Chemical Compound	Bioactivity
1.	Flavonoids	Antioxidant, antibacterial, anti-inflammatory
2.	Saponins	Antioxidant
3.	Alkaloids	Antioxidant
4.	Terpenoids	Antimicrobial, antioxidant, anti-inflammatory
5.	Terpenes	Antioxidant
6.	Phenols	Antioxidant
7.	Amino acids	Antioxidant
8.	Resins	Antioxidant, anticoagulant

Table 4. Specific phytochemical content of Mentawai taro corm based on GC-MS analysis (Santoso, 2022).

Sample	Chemical compound	% Area (relative levels)	Bioactivity
Mentawai Taro (*C. esculenta* L.)	Benzaldehyde, 3-chloro-5-methoxy-4-[(4-methyl phenyl) methoxy]	9,01	Anti-tumor
	Astaxanthin	51,39	Antioxidant, anti-inflammatory
	9-Octadecenoic acid	8,75	Antioxidant, a competitor for adipocyte lipid binding proteins
	1,5-anhydro-2,3,4,6-tetra-o-methyl-d-mannitol	2,56	Diuretic
	Taraxastrol	8,71	Anti-inflammatory

These compounds act as protectors against physiological damage caused by oxidative stress by influencing the increase in the Nrf2 pathway to produce antioxidant compounds and blocking the Nf-kB pathway, which is an inflammatory molecular signaling pathway (Pan Si and Zu, 2022). The saponin compounds found in taro corms act as antioxidants and influence the activity of microbiota in the digestive tract. Saponin compounds can prevent lipogenesis and produce SCFA, which influences the activation of the Bcl-2/Bax pathway leading to cell apoptosis (Santoso et al., 2019). The activity of taro flour phytochemical compounds in blocking the cell apoptosis pathway is evidenced in the data on the percentage of cell degeneration as shown in (**Table 1, 2**) which demonstrate significant differences between treatments.

This study established the neuroprotective effect of Mentawai taro (*C. esculenta* (L.) Schott) tuber flour against neurodegeneration in mice consuming a high-fat diet. We found that there are neurological health benefits of Mentawai taro tuber as a functional alternative food. Specifically, we observed a preservation of memory ability and curiosity levels associated with protection in neural areas of the brain such as the cerebral cortex and hippocampus, which play a role in cognitive activity.

In our current study, there are some limitations that need to be noted. Firstly, the results of MDA levels in the brain tissue of rats did not show significantly different results between the HFD group and the group fed with Mentawai taro flour, although other parameters were significantly different. This could be due to the fact that taro flour supports endogenous antioxidant activity in the body and is also expected to yield significant results if the test is conducted over a longer period of time; however, in this study, it was only conducted for 2 months. In addition, due to our limited resources and instruments, we only analyzed three samples in the measurement of MDA levels, thus not showing significant differences between treatment groups. Significant results may have been obtained if we analysed a larger number of samples. We are aware of the limitations of this study and recommend future researchers address this issue. Therefore, further research is needed to clarify these possibilities. The second limitation of our study is the absence of analysis of TNFα protein levels and antioxidant enzymes (such as SOD, CAT, GSH). These

data are important parameters to explain neuroinflammation due to HFD consumption, and the analysis of antioxidant enzymes may also support the conclusions of this study. However, in this study, we did not measure them due to resource and instrument limitations. We only included them as part of the discussion as one of the plausible mechanisms in HFD-induced neurodegeneration. Therefore, we acknowledge these limitations and suggest further in-depth studies related to this research for future researchers. Nonetheless, our study can serve as a foundational reference for further research and already provides scientific information regarding the protective effect of Mentawai taro corm against the incidence of neurodegeneration due to high-fat consumption.

Our research demonstrates that Mentawai taro flour *C. esculenta* (L.) Schott can effectively prevent cognitive and memory impairment in mice fed a high-fat diet in the Hebb William Maze Test and Hole Board Test, as shown in histopathological structure analysis. The mechanism of this prevention and preservation of cognitive conditions is through decreasing free radical levels by increasing endogenous antioxidant activity, thus protecting neurons in the hippocampus and cerebral cortex. Therefore, taro flour has the potential to be developed into a functional food or neuroprotective supplement against neurodegenerative diseases.

Acknowledgment

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Authorship Contribution

Fajri Ramadhan Marviano and Putra Santoso designed the experiments and prepared the manuscript. They were also responsible for the MDA, histopathology observation, and animal experiments, such as inducing a high-fat diet in mice. Resti Rahayu contributed to the data analysis and validation and revised the manuscript.

Ethical Declarations

In the current study, there is no study with human and human participants. All procedures involving the animals were approved by the Research Ethics Committee Faculty of Medicine, Andalas University (Approval No. 528/ UN.16.2/ KEP-FK/ 2021).

Conflict of Interest

The authors declare that they have no conflict of interest.

Financial Disclosure

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