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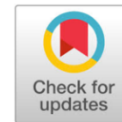
Original Research

Therapeutic potential of Cinnamomum burmannii bark extract in reducing Malondialdehyde (MDA) levels in MSG-induced wistar rats: a preclinical study



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Abstract: Increased consumption of monosodium glutamate (MSG) is associated with various health risks, including cardiovascular and neurological disorders. MSG triggers an increase in reactive oxygen species (ROS), the end product of lipid peroxidation produced when ROS increases is Malondialdehyde (MDA), On the other hand, interleukin 10 (IL-10) reduces the inflammatory effects in infectious conditions that can cause potential tissue damage. This study investigated the effect of cinnamon bark extract (*Cinnamomum burmannii*) on MDA and IL-10 levels in MSG-induced Wistar rats. Experiment with Post test only control group design was conducted. The number of samples was 24 male Wistar rats divided into 4 groups. KN healthy rats, K (+) rats were only induced by MSG, P1 rats were induced by MSG and given cinnamon bark extract at a dose of 100 mg, P2 rats were induced by MSG and given cinnamon bark extract at a dose of 200 mg. The average results showed a decrease in MDA levels after 14 days of treatment, one-way ANOVA test p = 0.001 (p <0.05) showed a significant difference in MDA levels KN 2.37 mg/ml ± 0.14, K+ 2.47 mg/ml ± 0.24, P1 2.32 mg/ml ± 0.20, and P2 0.84 mg/ml ± 1.07. Meanwhile, the average IL-10 levels showed no significant difference with one-way Anova test p = 0.127 (p <0.05) in the KN group, IL-10 levels were 93.25 pg / ml ± 25.01, K (+) 112.89 pg / ml ± 43.89, P1 69.48 pg / ml ± 12.83 and P2 93.29 pg / ml ± 12.11. Administration of cinnamon bark extract can reduce MDA levels in rats induced by MSG, but has no significant effect on IL-10 levels.

Keywords: Extract *Cinnamomum burmannii,* MDA Levels, IL-10 Levels, MSG.

INTRODUCTION

Monosodium glutamate (MSG) is one of the most widely used food additives, known for enhancing the palatability of foods and stimulating appetite.[1,2] MSG is commonly added to various processed foods, with the average daily intake varying across regions. For instance, in industrialized European countries, the average intake ranges from 0.3 to 1.0 g/day, with 0.58 g/day reported in the UK and 10.0 g/day in Germany.[3] In Nigeria, the intake is estimated at 0.56–1.00 g/day, whereas in Asia, it is significantly higher, ranging from 1.1–1.6 g/day in Japan, 1.5–3.0 g/day in Taiwan, and 1.6–2.3 g/day in South Korea.[3] The Food and Drug Administration (FDA) classifies MSG as a safe substance; however, some animal studies have highlighted adverse effects associated with chronic MSG

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consumption.[4] In Indonesia, the 2013 Riskesdas survey reported MSG consumption at 77.3%, alongside other dietary risk factors such as high intake of sugary foods (53.1%), fatty foods (40.7%), and coffee (29.3%).[5]

Excessive MSG consumption has been linked to numerous health risks, including cardiovascular, gastrointestinal, muscular, and neurological disorders.[1] Chronic MSG exposure has also been associated with asthma, obesity, cancer, diabetes, and oxidative stress.[6] Furthermore, it has been implicated in the pathogenesis of neurodegenerative diseases such as Parkinson's and Alzheimer's, as well as conditions like addiction, anxiety, stroke, depression, and epilepsy.[6] The detrimental effects of MSG are partly attributed to its role in increasing reactive oxygen species (ROS) and disrupting redox homeostasis, which can lead to systemic damage.[7] Elevated levels of malondialdehyde (MDA), a lipid peroxidation byproduct, signal increased oxidative stress and indicate damage to cell membranes due to free radicals.[8] Conversely, interleukin-10 (IL-10) plays a critical role in counteracting inflammation by reducing the effects of pro-inflammatory cytokines, thereby protecting tissues from damage and maintaining immune homeostasis.[9] This anti-inflammatory cytokine is essential in preventing chronic inflammatory conditions, which are often precursors to non-communicable diseases.[9]

Mitigating the adverse effects of excessive MSG intake requires dietary interventions rich in antioxidants.[6] Natural compounds with high antioxidant activity have emerged as promising alternatives for neutralizing ROS, repairing cellular damage, and restoring hormonal balance.[7] cinnamon bark extract, known for their antioxidant properties, may help mitigate ROS-induced damage and support cellular recovery.[10,11] In addition, cinnamon bark extract has garnered attention for its potential as an antioxidant additive in food and pharmaceuticals due to its robust antioxidant activity.[12] Studies have shown that cinnamon bark extract, administered at doses of 300, 400, and 500 mg/kg body weight, exhibits significant anti-inflammatory and analgesic effects, as evidenced by its ability to inhibit carrageenan-induced edema and reduce writhing in acetic acid-induced pain models.[13] Moreover, research on *Cinnamomum burmannii* extract demonstrates its hepatoprotective effects against multi-walled carbon nanotube (MWCNT) exposure by enhancing antioxidant status, reducing stress markers, and downregulating pro-inflammatory cytokines such as IL-6, IL-1β, Cox-1, and TNF-α.[14] This study aims to investigate the effects of cinnamon bark extract on MDA and IL-10 levels in male rats subjected to MSG induction, thereby exploring its potential as a natural antioxidant intervention.

MATERIAL AND METHOD

Laboratory experimental research on experimental animals with Post Test Only Control Group Design where this design was chosen to determine the effect of cinnamon bark extract on MDA and Il-10 levels analyzed after treatment. The subjects of the study used male white Wistar rats Rattus norvegicus aged 3-4 months with a body weight of 200-250 grams that met the inclusion and exclusion criteria. This study used 4 treatment groups, namely the normal group (KN) Wistar rats without MSG induction, the positive group (K +) namely Wistar rats induced by MSG, treatment group 1 (P1) Wistar rats induced by MSG and given cinnamon bark extract 100 mg / head, and treatment group 2 (P2) Wistar rats induced by MSG at a dose of 1g / head (200gr of rats) in 2ml aquadest and given cinnamon bark extract at a dose of 200 mg / head, all received oral treatment for 14 days. On the 15th day, blood was taken from all mice through the orbital sinus of the eye, then processed to obtain serum and MDA levels were measured by the Thiobarbituric acid assay (TBARS) method and IL-10 by the ELISA method.

Making Cinnamon bark extract

Cinnamon bark is obtained in plantations in the Kerinci area, Jambi Province because many cinnamon bark plants thrive, the bark is crushed using a smoothing machine then 1000 grams of powder is put into a dark container, stirred until homogeneous, closed immediately then stored in a room that is protected from sunlight for 5 days and often shaken. The soak is filtered with a flannel cloth, the pulp is washed with a solvent to a volume of 750 mL. The results are concentrated with a vacuum evaporator until a thick extract is obtained.[15]

Blood collection and serum collection

Blood collection is carried out through the vein of the eye using a capillary pipe. The blood is stored in a test tube and left for 15 minutes then in a centrifuge at 3500 rpm for 15 minutes, the serum that has been separated from the precipitate is then taken with a 100 µl pipette.

Procedure for measuring MDA levels TBARS method

MDA measurement on the 15th day after administration of cinnamon bark extract was examined using the Thiobarbituric acid assay (TBARS) method by taking 1 ml of mouse blood through the orbital sinus and then putting it into a centrifuge tube. Furthermore, the blood sample was centrifuged at a speed of 3000 rpm for 30 minutes, 500 µl of supermate was taken and then put into a centrifuge tube. Add 500 µl of 20% TCA solution and add 1% TBA solution in ¬50% glacial CH3COOH. Then heated in a water bath at a temperature of 95°C for 45 minutes. Then cooled to room temperature. Centrifuge speed 3000 rpm for 30 minutes. Take 500 µl of Filtrate using a micropipette. The color intensity is read spectrophotometrically at a wavelength of 532 nm.[16]

IL-10 level measurement procedure of elisa method

IL-10 measurement on the 15th day after administration of cinnamon bark extract according to each group. IL-10 level measurement was carried out using the Enzyme-Linked Immunosorbent Assay (ELISA) method, the stages are the standard solution and sample first at room temperature before use. The test is carried out at room temperature. Determine the number of strips needed for testing. Put the remaining strips into an aluminum zip for storage. Unused strips should be stored at 2-8°C. Add 50µl of standard to the standard well. Note: Do not add antibodies to the standard because the standard solution contains biotin-labeled antibodies. Add 40µl of sample to the sample well then add 10µl of IL-10 antibody to the sample label well, add 50µl of strettavidin-HRP to the sample well and standard well. Mix well. Cover the plate with a sealer. Incubate for 60 minutes at 37°C. Remove the sealer and wash the wells 5 times with a minimum of 0.3 ml wash buffer for 30 seconds to 1 minute for each wash. Add 50µl of substrate solution A to each well and then add 50µl of substrate solution B to each well. Incubate the sealed plate with fresh sealer for 10 minutes at 37°C in the dark. Add 50µl of Stop Solution to each well, the blue color will immediately change to yellow. Determine the Optical Density (OD) value of each well using a microplate reader set at 450 nm within 10 minutes after adding the stop solution.

RESULTS AND DISCUSSION

Analysis of the Effect of Giving Cinnamon Bark Extract on MDA Levels

The results of measuring MDA levels in each group are illustrated in table 1 and figure 1.

Table 1. Descriptive test, normality and homogeneity of MDA levels between treatment groups

Group	KN	K+	P1	P2	*p value*
Mean	2.37	2.47	2.32	0.84	
SD	±0.14	±0.24	±0.20	±1.07	
Shapiro wilk	0.95*	0.98*	0.95*	0.06*	
Levene test					0.046

Based on table 1, the results of the analysis, the average MDA of the normal group (KN) was 2.37 mg/ml ± 0.14, the positive group (K+) was 2.47 mg/ml ± 0.24, the average of treatment group 1 (P1) was 2.32 mg/ml ± 0.20 and treatment group 2 (P2) was 0.84 mg/ml ± 1.07.

The MDA level data in the four groups were all normally distributed (p>0.05) and also had a non-homogeneous data variance with a value of 0.046 (p>0.05). The lowest average MDA level was in the treatment group (P2), in the positive group (K+) mice induced by MSG experienced an increase in MDA levels, in treatment group 1 (P1) mice induced by MSG and given sungkai leaf extract at a dose of 100 mg MDA levels decreased, while in treatment group 2 (P2) mice induced by MSG and given cinnamon bark extract 200 mg/mouse experienced a significant decrease in MDA levels.

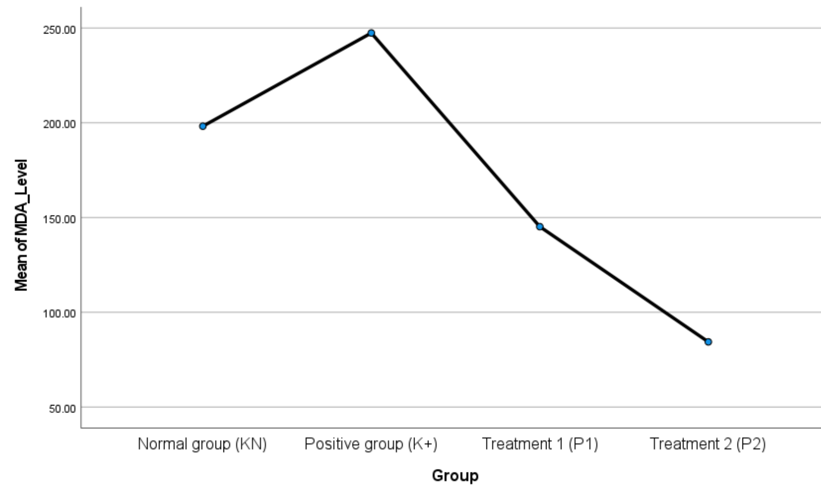

Figure 1. Graph of the average value of MDA levels by group

Based on the results of the one-way ANOVA test, a value of 0.001 (p<0.05) was obtained, indicating a statistically significant decrease in MDA levels among the treated groups. It was concluded that the administration of cinnamon bark extract could reduce MDA levels in MSG-induced mice. Determination of the dose of cinnamon bark extract that had the most effect on MDA levels was carried out.

Table 2. Difference in average MDA levels by group

Group	KN	K+	P1	P2
KN	-	0.971	0.998	0.180
K+	0.971	-	0.881	0.144
P1	0.998	0.881	-	0.197
P2	0.180	0.144	0.197	-

The results of the analysis of the average MDA levels of treatment group 2 (P2) which experienced a significant decrease in MDA levels compared to other treatment groups using the Tamhane post hoc test, obtained insignificant results when compared to KN, K+, and P1. It can be concluded that administration of 200 mg of cinnamon bark extract can reduce MDA levels in Wistar rats induced by MSG for 14 days.

Analysis of the Effect of Giving Cinnamon Bark Extract on IL-10 Levels

The results of IL-10 level measurements in each group are illustrated in table 3 and figure 2

Table 3. Descriptive tests, normality and homogeneity of MDA levels between treatment groups

Group	KN	K+	P1	P2	*p value*
Mean	93.25	112.89	69.48	93.29	
SD	±25.01	±43.89	±12.83	±12.11	
Shapiro wilk	0.877*	0.151*	0.955*	0.570*	
Levene test					0.050

Based on Table 3 and figure 2, the average IL-10 levels of the normal group (KN) were 93.25 pg/ml ± 25.01, the positive group (K+) 112.89 pg/ml± 43.89, treatment group 1 (P1) 69.48 pg/ml ± 12.83 and treatment group 2 (P2) 93.29 pg/ml ± 12.11.

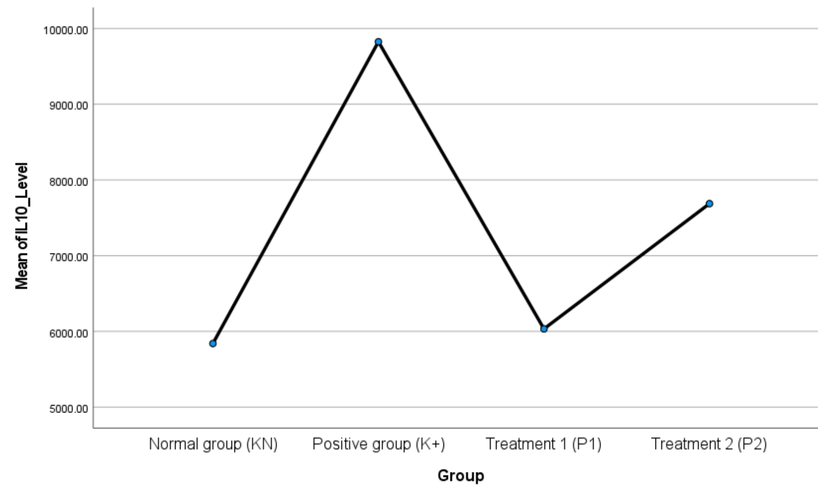

Figure 2. Graph of the average value of IL-10 levels in each group

The results of the analysis of the average IL-10 levels in the four groups were normally distributed (p>0.05), and had a non-homogeneous data variance with a value of 0.050 (p>0.05). The results of the one-way ANOVA test obtained a result of 0.127 (p<0.05) which means there is no difference in the average IL-10 levels between the four groups. It can be concluded that the administration of cinnamon bark extract has no effect on increasing IL-10 levels in MSG-induced Wistar rats.

Monosodium glutamate (MSG) is associated with various dangerous side effects. According to research, MSG has been linked to metabolic and digestive anomalies affecting the nervous, pulmonary, and circulatory systems. Damage to the hypothalamic nuclei, particularly the arcuate and ventromedial nuclei, was observed in newborn mice exposed to MSG. This damage resulted in increased body weight, fat deposition, reduced motor activity, and decreased growth hormone secretion.17,18 MSG shows a functional range at concentrations between 0.2-0.8%, with excessive amounts negatively affecting taste. The maximum tolerable dose for enhancing taste in humans is 60 mg/kg body weight (BW). The WHO estimates that 200,000 tonnes of MSG are produced annually, with daily consumption reaching up to 3 grams in some Asian countries.[19] These widespread consumption patterns underscore the need for further investigation into MSG's potential adverse effects on human organ systems.

The global increase in MSG consumption is driven by changing dietary habits, urbanization, improved living standards, and the expanding food processing industry in many Asian countries.[18] To counteract MSG's adverse effects, the role of antioxidants becomes critical. Antioxidants protect against free radicals and mitigate damage.[20] Cinnamon is a notable source of antioxidant compounds, including cinnamaldehyde, cinnamic alcohol, and cinnamic acid, which possess antioxidant, anti-inflammatory, and antibacterial properties. These compounds

have been used to treat diabetes and cardiovascular diseases.[21] An antioxidant-rich diet offers significant benefits, reducing oxidative stress and inflammation, both of which are linked to various metabolic disorders, including hyperglycemia.[10,22]

Research indicates that administering cinnamon bark extract at a dose of 200 mg/rat (treatment group P2) significantly reduces malondialdehyde (MDA) levels compared to other groups. This aligns with Handayani's (2023) findings that cinnamon bark ethanol extract improves lipid profiles due to its cinnamaldehyde and quercetin content, which inhibit HMG CoA reductase activity. Additionally, flavonoids, tannins, and other compounds in cinnamon reduce triglycerides and MDA levels.[23] Similarly, Perisnawati (2024) demonstrated the effectiveness of cinnamon bark extract in lowering MDA levels in hyperglycemic mice, with the best results at a dose of 100 mg/kg BW.[24] These reductions are attributed to the extract's antioxidant components, which combat oxidative stress, inhibit reactive oxygen species (ROS) production, and enhance antioxidant response pathways by activating nuclear factor erythroid 2–related factor 2 (NRF-2) and suppressing nuclear factor-kappa B (NF-KB).[25,26]

In treatment group P1, where cinnamon bark extract was administered at 100 mg/rat, no significant decrease in MDA levels was observed. This may be due to the high oxidative stress induced by excessive MSG, which overwhelmed the antioxidant capacity of the cinnamon extract. Inadequate antioxidants can fail to counteract free radicals, leading to oxidative stress and cellular damage.[27] MDA serves as a key marker for lipid peroxidation and cell membrane damage caused by oxidative stress. Elevated MDA levels indicate increased ROS activity, which can trigger cell death.[28]

The lack of significant differences in MDA levels among the healthy (KN), positive control (K+), and P1 groups could be influenced by various factors, including age, genetics, and environmental conditions, which impact the body's endogenous antioxidant levels.[29] Cinnamon bark extract has been shown to improve mitochondrial and endoplasmic reticulum inflammation caused by oxidative stress. Its active components enhance total antioxidant capacity and reduce lipid peroxidation, thereby mitigating tissue damage.[30] Oxidative stress can be countered through various mechanisms, with the antioxidant defence system being the most effective.[31]

Despite the observed benefits of cinnamon bark extract, no significant effect was seen on IL-10 levels in Wistar rats exposed to a toxic MSG dose of 1 gram/day for 14 days. IL-10 is an anti-inflammatory cytokine crucial for immune regulation and prevention of chronic inflammation.[32] The lack of significant change in IL-10 levels may be due to the acute phase of the experiment, as systemic treatment for 14 days might not have been sufficient to elicit noticeable effects on this parameter.[33]

This study did not conduct a detailed phytochemical analysis of the specific antioxidant components in the cinnamon bark extract, which could influence the MDA level analysis results. Baseline analyses prior to treatment would be necessary to compare pre- and post-treatment levels. Future studies could optimize MSG and cinnamon extract doses to enhance the observed effects. Adjusting MSG induction and increasing the cinnamon extract dose above 200 mg/rat may yield more pronounced outcomes.

CONCLUSION

This study highlights the harmful effects of monosodium glutamate (MSG) on metabolic, digestive, and nervous systems, primarily through oxidative stress, as evidenced by elevated malondialdehyde (MDA) levels. Cinnamon bark extract shows promise as a natural antioxidant, significantly reducing MDA levels, indicating its ability to mitigate oxidative damage. However, at lower doses the effects were not significant, and no notable changes were observed in IL-10 levels,

likely due to the short duration of the study. These findings suggest that cinnamon bark extract could serve as a protective agent against MSG-induced oxidative stress. Future research should focus on optimizing doses, evaluating long-term effects, and conducting human trials to confirm its efficacy.

AUTHORS' CONTRIBUTIONS
Dina Afrianti is the head of the TPP who coordinates with team members for the smooth running of the research process and writing of this scientific publication, Wahyudi is the research implementer at the IBL FK Unissula laboratory, Ririh Jatmi Wikandari is in charge of processing laboratory data, Rodhi Hartono is the journal reviewer and supervisor, Erisa Febriyani is the TPM chairman who designed the research flow, Egy Sunanda Putra as a TPM member whose job was to help the TPM chairman design the research flow. All authors have read and approved the final journal entry.

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DATA AVAILABILITY STATEMENT
The utilized data to contribute to this investigation are available from the corresponding author on reasonable request.

DISCLOSURE STATEMENT
The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any affiliated agency of the authors. The data is the result of the author's research and has never been published in other journals.

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