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RESEARCH ARTICLE OPEN ACCESS

The Role of Quercetin in Mitigating the Oxidative Stress and Hepatotoxicity Induced by Monosodium Glutamate (MSG) in Male Albino Rats

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Abstract

Objective: Monosodium glutamate (MSG) is a widely used food additive, but high-dose exposure has been linked to liver toxicity. This study assessed the protective effects of quercetin on MSG-induced hepatotoxicity in male albino rats.

Methods: Twenty male Sprague Dawley rats (200–250 g) were divided into four groups (n = 5/group). Group 1 received distilled water (control); Group 2 received quercetin (100 mg/kg/day) for three months; Group 3 received MSG (15 mg/kg/day) for three months; Group 4 received MSG for one month, followed by a 48-hour washout, then quercetin (100 mg/kg/day) for one month. Serum levels of malondialdehyde (MDA), total antioxidant capacity (T-AOC), tumour necrosis factor-alpha (TNF-α), and liver enzymes (ALT, AST, ALP, GGT) were evaluated.

Results: MSG significantly increased MDA (3.65 ± 0.26 nmol/mL), TNF-α (3.71 ± 0.98 pg/mL), ALT (56.86 ± 3.64 U/L), AST (65.26 ± 3.65 U/L), ALP (146.10 ± 8.32 U/L), and GGT (5.84 ± 0.36 U/L), while decreasing T-AOC (2.76 ± 0.32 U/L) ($p \leq 0.05$). Group 4 showed marked improvement: reduced MDA (2.78 ± 0.31 U/L), TNF-α (2.78 ± 0.37 pg/mL), ALT (21.75 ± 2.33 U/L), AST (31.54 ± 3.78 U/L), ALP (65.73 ± 6.42 U/L), GGT (2.99 ± 0.35 U/L), and increased T-AOC (2.78 ± 0.48 µmol/mL).

Conclusion: Quercetin significantly reduced MSG-induced oxidative stress, inflammation, and liver enzyme elevation. These findings support its potential as a natural hepatoprotective agent.

Keywords: Quercetin, Monosodium Glutamate (MSG), Oxidative stress, Inflammation, Hepatotoxicity

Plain English Summary

This study explored how quercetin, a natural compound found in fruits and vegetables, can help protect the liver from damage caused by monosodium glutamate (MSG), a common food additive used to enhance flavour. While MSG makes food tastier, research suggests that consuming high amounts over time may harm the liver and increase inflammation and oxidative stress (damage caused by unstable molecules in the body). Researchers tested this in male albino rats by dividing them into four groups: one group was given distilled water (control), another got quercetin, the third received MSG, and the fourth received MSG followed by quercetin treatment. After several weeks, they examined the rats' blood and liver to measure markers of liver damage, inflammation, and antioxidant levels. The results showed that rats treated with MSG alone had higher levels of liver enzymes, a molecule called TNF-α (a marker of inflammation), and

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MDA (a marker of oxidative stress). Their total antioxidant levels dropped significantly. In contrast, rats that were later treated with quercetin showed much better outcomes, lower liver damage, less inflammation, and improved antioxidant levels, compared to the MSG-only group.
In summary, quercetin helped reduce the harmful effects of MSG in rats. This suggests quercetin could be a safe, natural option to protect the liver from certain types of chemical damage. It may also serve as an alternative or complement to conventional drugs used in treating liver-related health issues.

Introduction

One of the most crucial substances used to enhance the chemical and sensory qualities of food items is a flavour enhancer. They contribute to the improvement of processed foods' flavour after part of it has been lost during processing. Additionally, they frequently prolong their shelf life (1). Substances added to food to provide unique flavours to compensate for flavour loss during processing are also referred to as flavour enhancers. Flavour enhancers, which have serial numbers ranging from E600 to E699, improve the flavour of food. Chemical salts make up most of them. Taste and flavour are essential for enjoying food. Despite having essential minerals, food containing little flavour is typically discarded (2). To provide unique flavours to meals with little nutritional value, flavour enhancers are utilised. Monosodium glutamate (MSG), commonly referred to as Chinese salt, is the most well-known of them (3).

According to Kasmara (4), Glutamate is the most prevalent non-essential amino acid in the body, and it exists in two primary forms: free glutamate and bound glutamate. Many foods, such as meat, fish, poultry, milk, and vegetables, naturally contain glutamate; the amount of free glutamate in vegetables is greater. Traditional sauces and spices are among the numerous prepared and processed meals that contain glutamate (5). Originally originating in Asia, monosodium glutamate (MSG) has a unique flavour that is most prevalent there. Along with sweet, sour, salty, and bitter, it is regarded as the fifth fundamental flavour and is well-known in Western cultures (6). As a flavouring and flavour enhancer, monosodium glutamate is one of the most often used food additives worldwide. The US Food and Drug Administration (FDA) claims that despite the health risks, food makers are eager to continue using it since it tastes nice and is affordable (7).

Although monosodium glutamate is widely used as a food flavouring agent to increase appetite and taste, research has shown that it can have toxic effects on laboratory animals, particularly at high doses, as well as humans through adverse effects on the kidneys, liver, and testes (8).

An increasing number of people all over the world are interested in medicinal and aromatic plants. This highlights the significance of these plants in both medicine and traditional use. There is a focus on planting and developing these plants using biotechnology to maximise their use. Most people are turning to nature for an answer and rely on alternative medicine to avoid the side effects that chemical medicines and drugs present after some time of use. In addition, most of the aromatic and medicinal plants have multiple uses and functions. They are a significant source of active compounds in most medicines and drugs and find use in food as spices and oils that are highly nutritious, as well as in the production of the best healthy cosmetics, perfumes, and incense. They are also used in landscaping and decor, and a newer worldwide trend is to use plant extracts (9).

Quercetin is a pigment found in plants that is a member of the flavonoid group. Numerous plants, including berries, apples, onions, green tea, ginkgo, and others, contain it. Quercetin is similarly abundant in buckwheat tea (10). As one of the most prevalent antioxidants in the diet, quercetin offers several health advantages. It is crucial and effective in assisting the body in fending off damage from free radicals, which are linked to some chronic illnesses, including heart disease, degenerative brain problems, and some forms of cancer. Additionally, it can help decrease blood pressure, reduce inflammation, and relieve allergy symptoms (11). Therefore, the current study aimed to evaluate the therapeutic efficacy of Quercetin in male albino rats to combat Monosodium Glutamate (MSG), by studying some physiological parameters in the rats' liver.

Recent research by Kasahara et al. (10) has highlighted the hepatoprotective potential of quercetin through its modulation of gut microbiota and systemic inflammation, which supports its role in reducing hepatic oxidative stress and pro-inflammatory cytokine expression. Unlike earlier studies that focused on isolated oxidative or inflammatory outcomes, this study simultaneously evaluates multiple interrelated biochemical parameters—including total antioxidant capacity (T-AOC), lipid peroxidation (MDA), inflammatory cytokines (TNF-α), and liver enzyme activity, providing a more integrated understanding of MSG-induced hepatotoxicity and the protective role of quercetin. This study was designed to evaluate the therapeutic efficacy of quercetin in mitigating oxidative stress and hepatotoxicity induced by monosodium glutamate (MSG) in male albino rats. We hypothesised that quercetin administration would significantly reverse MSG-induced biochemical alterations, specifically by restoring antioxidant capacity, reducing lipid peroxidation (MDA), and suppressing inflammatory cytokine levels (TNF-α).

Materials and Methods

Animals used in the study

The study, which lasted three months from November to January, involved twenty adult male albino rats of the Sprague Dawley type. It was carried out in the animal house of the Department of Life Sciences, College of Education for Pure Sciences, University of Anbar. Their weights varied from 200 to 300 g, while their ages ranged from 3 to 4 months.

A minimum of five animals per group was selected based on similar hepatotoxicity models and in line with ethical considerations to reduce animal use. Given the anticipated moderate-to-large effect sizes, this sample size was sufficient to detect differences using one-way ANOVA at $p \leq 0.05$, though we acknowledge this as a limitation in terms of statistical power.

Materials used in the experiment

Monosodium glutamate and quercetin were purchased from Sigma USA.

The experimental design

The animals were divided according to similar weights into four groups, each containing five animals. The first group, the control group, received an oral dose of 5 mL/kg distilled water. The second group received an oral dose of quercetin (100 mg/kg) daily at a dose of 2 ml for three months. The third group received an oral dose of monosodium glutamate (15 mg/kg) daily at a dose of 2 ml for three months. The fourth group received an oral dose of monosodium glutamate (15 mg/kg) daily at a dose of 2 ml for one month, then was left for 48 hours, after which it received an oral dose of quercetin (100 mg/kg) daily at a dose of 2 ml for one month.

The dosing regimen for MSG (15 mg/kg) was selected based on Abdou et al. (12), who observed consistent oxidative and hepatotoxic effects at this level. Quercetin dosing (100 mg/kg) was based on Alharbi et al. (13), where significant antioxidant and anti-inflammatory effects were demonstrated in rodent models.

Collection of blood samples:

The animals underwent 24 hours of hunger once the trial was over. The next day, an intraperitoneal injection of 0.1 ml/100 g of body weight of ketamine/xylazine was used to put them to sleep. Following that, sterilised, disposable 5 ml syringes were used to take blood samples straight from the heart. After being drawn into a white tube, the blood was centrifuged for 15 minutes at 3,000 rpm. Micropipettes were then used to separate the serum, which was subsequently kept at -20°C in white plastic test tubes. Before biochemical testing, all relevant data for every sample were documented.

Assay of oxidative stress and antioxidants

The level of (T-AOC and MDA) in blood serum was estimated using a ready-made test kit provided by the American company Elabscience, using the colourimetric method on a spectrophotometer.

Measurement of the level of Tumour Necrosis Factor Alpha (TNF-α) in the blood serum

Using an ELISA Microplate Reader and a pre-made test kit from the American company Elabscience (www.elabscience.com, No: E-EL-H0109), serum TNF-α levels were determined using the Sandwich ELISA technique.

Liver function test

The enzyme levels (ALT, AST, ALP, GGT) were measured in blood serum using a ready-made test kit provided by the Spanish company Linear, using the UV enzymatic method on a Spectrophotometer.

Statistical analysis

GraphPad Prism V.8.1 was used to statistically analyse the findings and determine whether there was a significant difference between the values of the treated groups. Group comparisons following ANOVA were conducted using Duncan's multiple range test to identify statistically significant differences among group means at the 0.05 significance level. While Tukey's HSD is more conservative, Duncan's test was selected for its sensitivity in small-sample, exploratory studies (14).

Results

Estimation of oxidative stress and antioxidants in the blood serum of male rats

Figure 1 shows the effect of quercetin on oxidation factors. We note an increase at the probability level ($p \leq 0.05$) in the activity of (MDA) Malondialdehyde in the male rats of the third group orally dosed with (MSG) nmol/mL (3.652 ± 65.26), when compared with the control group (561.2 ± 50.28 nmol/mL). There was, however, a decrease noted in the activity of (MDA) in the second group orally dosed with (Quercetin) (680.2 ± 45.28), compared with the control group. There was a decrease in (MDA) observed in the fourth group (3.778 ± 54.31), compared to the third group dosed with (MSG); on the other hand, a significant decrease in the level of (MDA) is observed in the second group dosed orally with (Quercetin).

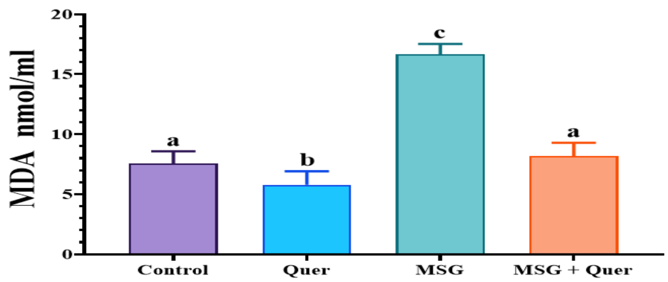

Figure 1: The effect of quercetin on the level of Malondialdehyde (MDA) in the blood serum of male rats treated with monosodium glutamate

The effect of quercetin on total antioxidant capacity (T-AOC) is illustrated in Figure 2. Comparing the total antioxidant capacity in male rats of the second group (ml/μmol) with that of the control group (ml/μmol) (29±0.49), a significant rise was observed at the level of probability (P≤0.05). But in comparison with the control group, the results of the statistical analysis showed a very abrupt, considerable reduction in the overall antioxidant capacity of male rats from the third group (2.760±31.96) at the level of probability (P≤0.05). The fourth male rat group (ml/μmol) (2.778±47.52), treated orally with monosodium glutamate (MSG) and quercetin, had significantly higher antioxidant capacity than the third group (MSG), according to the results of statistical analysis.

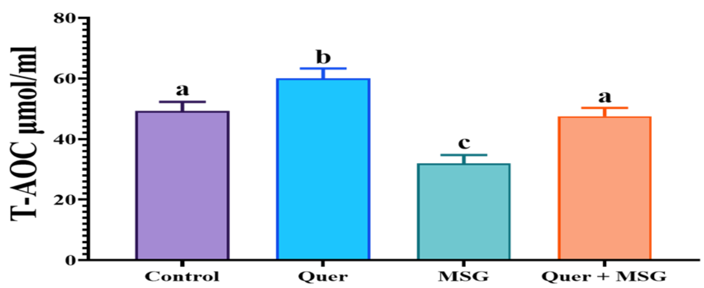

Figure 2: The effect of quercetin on the level of the total antioxidant capacity (T-AOC) in the blood serum of male rats treated with monosodium glutamate

Effect of monosodium glutamate on the level of TNF-α in the serum of male rats treated with quercetin

Male rats in the third group had a higher level of TNF-α (pg/ml; 3.705±56.98) at the probability level (P≤0.05) than the control group (2.547±33.45) pg/ml, as shown in Figure 3. In contrast, the male rats in the second group showed a reduction in the level of TNF-α at the probability level (P≤0.05) (3.230±28.83) pg/ml compared to the control group. Also, there was an observable reduction in the level of α-TNF in the fourth group (2.778±37.15) pg/ml as compared to the third group, which received an MSG dosage. It was noticed that there was a reduction in the amount of TNF-α activity in the male rats of the second group that received an oral dosage of quercetin.

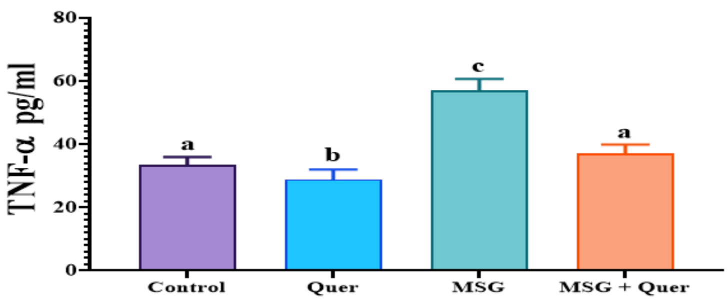

Figure 3: The effect of quercetin on the level of TNF-α in the blood serum of male rats treated with monosodium glutamate

Effect of monosodium glutamate on the level of liver function in the serum of male rats treated with quercetin

Table 1 illustrates the effects of quercetin on liver function. Comparing the blood serum of male rats in the third group that received an oral dosage of monosodium glutamate (MSG) to the control group, we see a substantial rise in the activity level of the enzymes (ALT), (AST), (ALP), and (GGT) at the probability level ($P \leq 0.05$). There was a reduction in liver enzyme activity at the probability level ($P \leq 0.05$) in the second group that received an oral dosage of quercetin. Comparing the male rats in the fourth group, who received oral doses of MSG followed by quercetin, respectively, to the third group, the same outcome was seen.

Table 1: The effect of quercetin on the level of liver function in the blood serum of male rats treated with monosodium glutamate

		Control	Quercetin	MSG	MSG + Quercetin
ALT U/L	Mean	18.01[a]	17.04[a]	56.86[b]	21.75[a]
	± SD	±3.208	±3.344	±3.643	±2.334
AST U/L	Mean	28.50[a]	28.45 [a]	65.26 [b]	31.54 [a]
	± SD	±2.561	±2.680	±3.652	±3.778
ALP U/L	Mean	59.60 [a]	58.57 [a]	146.1 [b]	65.73 [a]
	± SD	±6.421	±6.592	±8.320	±6.420
GGT U/L	Mean	3.558 [a]	2.957 [b]	5.837 [c]	2.989 [d]
	± SD	±0.402	±0.355	±0.362	±0.350

Mean values within a column not sharing a common superscript letter (a, b, c and d) were different, $p < 0.05$

Discussion

The current study's findings demonstrated that administering rats MSG at a dose of 15 mg/kg caused the average levels of total antioxidants in the body to reduce ($P \leq 0.05$), while increasing the average level of MDA (Figure 1). This outcome aligned with other research findings, which showed that administering MSG to rats resulted in oxidative stress by raising MDA levels and lowering antioxidant levels (15). However, research found that rats exposed to MSG regularly experienced harm to their liver and kidneys because of elevated amounts of free radicals and oxidative stress (12). Reactive oxygen species (ROS) and reactive nitrogen species (RNA), which are crucial in oxidative stress, are produced when monosodium glutamate is consumed. Cancer, neurodegeneration, diabetes, heart disease, renal disease, liver damage, and the development of cirrhosis can result from this. In addition to causing necrosis and apoptosis, oxidative damage to proteins, lipids, and DNA also intensifies the inflammatory response, which starts fibrosis. Additionally, ROS causes Kupffer cells and circulating inflammatory cells to produce more proinflammatory mediators (16). This might help to explain why MSG is seen as a stressor.

Lipid peroxidation, which is a crucial sign of oxidative damage brought on by reactive oxygen species (ROS), is shown by elevated MDA. This implies that consuming MSG causes the body to produce more free radicals. MDA is created when these free radicals oxidise polyunsaturated fatty acids to lipid peroxidation. This causes oxidative stress and may harm several organs by breaking cell membranes and upsetting the equilibrium between oxidants and antioxidants (17). According to one study, MSG mediates this process by raising intracellular Ca^{2+} levels, which either encourages lipid peroxidation or phospholipid degeneration (18).

According to a study, the population's elevated risk of cardiovascular disease is brought on by a rise in monosodium glutamate intake, which lowers total antioxidant capacity (T-AOC). Our study's findings, which revealed a marked decline in antioxidants, suggested that this risk could be related to rising meat consumption and processed meats that include it (19). Elevated MDA levels suggest that MSG may be the cause of this, as it increases oxidative stress by generating more free radicals. According to our present research, oxidative stress is the cause of the elevated MDA levels in the MSG-treated groups. The production of reactive oxygen and nitrogen species, including hydrogen peroxide, nitric oxide, peroxynitrite, and superoxide anion, which lower antioxidant levels, is the main cause of the risk of MSG toxicity. MDA is created when polyunsaturated fatty acids are oxidised by these free radicals to lipid peroxides. This leads to oxidative stress by damaging cell membranes and upsetting the equilibrium between oxidants and antioxidants.

By reducing MDA levels because of higher antioxidant levels, the Quercetin extract was found to help decrease lipid peroxidation levels in the groups that received it. By scavenging free radicals and blocking lipid peroxides in membranes that induce cell necrosis, these antioxidants help to maintain a balance between oxidants and cells. It also helped to rearrange the architecture of cells. Quercetin is an antioxidant that may scavenge free radicals.

The injection of quercetin, a potent antioxidant, is responsible for the rise in antioxidant levels in MSG treatments, either alone or in combination (20). According to our study's findings, the second group's total antioxidant capacity was much higher than that of the control group, and the fourth group's was higher than that of the third. Alharbi et al. (13) reported an increase in total antioxidant capacity (T-AOC) in the group of animals treated with quercetin. These results are consistent with our findings, indicating that long-term quercetin consumption protects neurons from the damaging effects of oxidative stress caused by ageing and helps support memory function in elderly male rats. This may be due to quercetin enhancing the body's antioxidant systems, which in turn improve overall organ function.

The results of our current study showed an increase in the level of tumour necrosis factor (TNF-α) in the animals of the third group treated with MSG. This may be due to the increased production of ROS in the endogenous formation of cells. Much evidence indicates that pathophysiological concentrations of endogenous TNF-α stimulate tumour formation and growth. Cancer is associated with elevated expression of the cytokine (TNF-α), which is produced in the tumour microenvironment by cancer cells and stromal cells (21).

Tumour necrosis factor alpha (TNF-α) is an active proinflammatory cytokine, and its activity increases in acute inflammation caused by proinflammatory cytokines. It is also a key mediator of various physiological processes, including cell proliferation, apoptosis, insulin resistance, and the functions of cells that line blood vessels. Different types of cells in the body contain TNF-α, which is generated in the liver primarily by Kupffer cells (22). The results of our current study, as shown in Figure 3, confirmed an increase in the level of tumour necrosis factor α-TNF in the animals of the third group treated with MSG. This is consistent with many studies that have proven that the increase in TNF-α is directly or indirectly related to MSG consumption (23, 24). The reason may be attributed to the production of free radicals that react under certain conditions to form nitroso compounds, as these compounds are inflammatory substances. Much evidence indicates that pathological physiological concentrations of endogenous TNF-α stimulate tumour formation and growth, as cancer is associated with high expression of the cytokine (TNF-α) that is produced in the tumour microenvironment by cancer cells and stromal cells (25).

The results of our current study showed a decrease in the level of TNF-α in the serum of rats in the group treated with MSG and quercetin compared to the third group dosed with MSG. This is due to the anti-inflammatory and anti-tumour activity of quercetin, which had an inhibitory effect on cancer cell migration and an effect on programmed cell death in cancer cells (18). Our current study is consistent with a study that confirmed the preventive and therapeutic role of quercetin in many pathogens due to its anti-inflammatory properties (26). Our study was consistent with what was stated by a study that indicated a decrease in the level of TNF-α because of the use of quercetin in rats treated with carbon tetrachloride, and this compound showed high anti-inflammatory activity (27).

Exposure to these toxins can cause several illnesses because the liver is the main site of metabolism and a significant detoxifying organ. Cellular enzymes released into the circulation by damaged liver cells can be evaluated by blood testing. The primary liver enzymes, ALT and AST, are elevated in the blood at the same time, which suggests a high likelihood of liver injury. One of the primary causes of liver disorders, which can range in severity from cirrhosis to liver cell necrosis and enzyme leakage, is oxidative stress brought on by free radicals (28).

An essential clinical sign of liver function and a key indicator of liver cell integrity is the measurement of liver enzyme activity in serum. Hepatic enzymes may be released into the circulation because of hepatocyte cell membrane degradation. In the present investigation, MSG-treated animals exhibited several harmful functional alterations (Table 1). \The hepatocyte necrosis brought on by oxidative stress and an increase in free radicals may be the source of the raised liver enzymes in the rats' serum in our current investigation. This might result in the oxidation of lipids in the cell membrane and the release of enzymes into the blood. Effective reactions between the NO radical and oxygen result in the production of various oxidants and nitro compounds, including peroxynitrite, which damages the liver and contributes to hepatocyte mortality (13).

These findings are in line with research that found that male rats given monosodium glutamate had higher levels of the enzymes GGT, ALT, AST, and ALP, indicating alterations in the treated rats' livers as compared to the control group (12). Consuming MSG may stimulate the production of free radicals, which damage liver cells' plasma membranes, inducing cell damage and the subsequent release of these enzymes into the bloodstream (15). This could be the cause of the rise in these enzyme levels. Increased reactive oxygen species cause oxidative stress, which breaks down the DNA, proteins, and lipids in liver cells. This causes the cells to degenerate or necrotise, which is followed by their demise and the release of their contents into the circulation.

When MSG is consumed continuously, the liver of infected animals undergoes further alterations because of increased oxidative stress generated by the buildup of free radicals, which causes the liver cells to collapse and lipid peroxides to accumulate in the cell or mitochondrial membranes. This causes sinusitis to worsen, inflammatory regions to develop, and poor venous flow at the level of the hepatic vein, or inferior vena cava (29).

Additionally, the data show that the group of rats given MSG and treated with cristin had much lower liver enzyme activity. This outcome aligns with the findings of Saeed et al. (30). As our study demonstrated, the effectiveness of cristin as a natural antioxidant that analyses and scavenges free radicals and inhibits the oxidation-induced destruction of cell membranes may be the cause of this decline. This protects liver tissue from damage and stops enzymes from escaping into the bloodstream. The enhanced antioxidant efficacy brought about by our study's findings not only prevented lipid peroxidation, which shielded cell walls from necrosis, but also preserved cell function by halting the release of liver enzymes into the bloodstream, repairing and shielding cells from harm, and boosting the liver's synthesis of proteins that hasten the process of self-renewal and the development of new liver cells.

Quercetin's hepatoprotective effects may be attributed, in part, to its ability to activate the Nrf2 (nuclear factor erythroid 2-related factor 2) signalling pathway, which upregulates the expression of endogenous antioxidant enzymes such as glutathione peroxidase and superoxide dismutase (13). This activation enhances the liver's resilience against reactive oxygen species generated by MSG exposure

Study limitations

A key limitation of this study is the absence of histopathological examination of liver tissue, which would have added anatomical and cellular insights to the observed biochemical changes. Additionally, the small sample size and lack of gene/protein-level assessments (e.g., Nrf2 pathway markers) limit the depth of mechanistic interpretation. Although this study focused on biochemical parameters of liver function and oxidative stress, histological analysis of liver tissue was not performed. Future studies should prioritise incorporating histopathological evaluation of liver tissue alongside biochemical assessments to provide a more comprehensive understanding of cellular and structural changes associated with MSG toxicity and quercetin's protective effects

Conclusion

The current study's findings showed that male albino rats exposed to monosodium glutamate (MSG) over an extended period had higher levels of liver enzymes (ALT, AST, ALP, and GGT), higher levels of oxidative stress (MDA) and inflammation markers (TNF-α), and lower antioxidant capacity (AOCT). In comparison to the MSG-only group, quercetin therapy markedly improved these parameters, resulting in lower levels of enzymes and indicators of oxidative and inflammatory damage as well as an increase in antioxidant capacity. According to these results, quercetin is a safe natural option that may help avoid liver diseases since it has promising therapeutic qualities in reducing the harmful physiological consequences linked to long-term MSG exposure.

List of Abbreviations
MSG**:** Monosodium glutamate
AOCT: Total antioxidant capacity
MDA: Malondialdehyde

Declarations

Ethics approval and consent to participate
All animal procedures were approved by the Ethical Approval Committee of the University of Anbar, following international guidelines for the care and use of laboratory animals. The study was granted official approval under Reference Number: 241, dated 26/12/2024. All experimental protocols were reviewed and endorsed by the College of Education for Pure Sciences, Department of Biology, University of Anbar. Efforts were made to minimise animal suffering and the number of animals used, per the principles of Replacement, Reduction, and Refinement (3Rs).

Consent for Publication

Availability of Data
Data for this work is available from the authors and may be provided upon reasonable request.

Conflicts of Interest
None.

Funding
None.

Authors' contributions
FRK: Conceptualisation, Experimental Design, Data Collection, Laboratory Analysis, Statistical Analysis, Interpretation of Results, Drafting and Writing the Manuscript.
AHL: Supervision, Guidance on Methodology, Critical Review and Editing of the Manuscript, Final Approval of the Version to Be Published.
Both authors have read and approved the final manuscript.

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