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Quercetin and *Gongronema Latifolium* Ameliorated IL-1β and TNF-A Mediated Neurobehavioural Deficits and Neuroinflammation Following Lead Administration in Male Wistar Rats

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ABSTRACT

Lead neurotoxicity remains a critical public health concern, causing oxidative stress, neuroinflammation, and cognitive deficits in exposed populations. This study investigated the comparative neuroprotective effects of quercetin and *Gongronema latifolium* in male Wistar rats exposed to lead acetate (50 mg/kg/day) for 28 days. Thirty adult male rats were randomly assigned to six groups, including control, lead-only, quercetin-treated (500 mg/kg), and *Gongronema*-treated groups at 250, 500, and 1000 mg/kg. Neuroinflammatory markers (TNF-α and IL-1β) were quantified via ELISA, while neurobehavioral performance was assessed using the Y-maze test, focusing on total arm entries as a measure of exploratory behaviour. Lead exposure significantly increased TNF-α and IL-1β compared with controls ($p<0.05$), confirming pronounced neuroinflammation. These markers were significantly reduced to near-control levels by high-dose Gongronema and quercetin (1000 mg/kg and 500 mg/kg, respectively; $p < 0.05$), thereby demonstrating the high potency of these compounds as anti-inflammatory agents. In the Y-maze, total arm entries differed significantly between groups ($F=4.536$; $p=0.015$), with high-dose *Gongronema* and quercetin improving exploratory behaviour. The results of the study reveal that high-dose *Gongronema latifolium* and quercetin can effectively alleviate neuroinflammatory complications and partially restore hippocampus-dependent cognitive function in lead-exposed subjects. The therapeutic potential of these natural compounds as effective, cost-free interventions for environmental neurotoxicity is thus established.

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1. INTRODUCTION

Though invisible, lead poses serious risks to brain health, altering how people think, act, or move. Found nearly everywhere in polluted environments, it spreads easily, hitting hardest in regions with weak safety rules (World Health Organisation [WHO], 2024). Once inside the body, this metal slips into the brain without much resistance, triggering chaos through cell stress, swelling in neural tissue, and harm to nerve cell results seen clearly in struggles with remembering, thinking fast, or coordinating motion (Mason et al., 2014; Harshitha et al., 2024; Liu et al., 2019). Research relying on male Wistar rats which mirror human nervous system reactions closely shows repeated patterns: lead ramps up damaging molecules called ROS, interferes with signal transmission between neurons, while also waking support cells that pour out inflammatory signals like TNF-α, IL-1β, and IL-6, worsening mental performance and behaviour (Fathabady et al., 2021; Shvachiy et al., 2021; Bokara et al., 2008).

Exposure to lead triggers toxic reactions in the nervous system, extending beyond individual neurons to affect overall health. Even when research zooms in to the smallest biological levels, real-world impacts become obvious over time. Kids exposed to lead for extended periods usually score below average on intelligence tests - trouble concentrating and behavioural issues often appear too. Adults, too, face risks - mental sharpness may diminish over time, sometimes progressing toward degenerative brain conditions. Research

links such exposure directly to mechanisms tied to Alzheimer's disease. Lab-based studies support that when organisms encounter lead, they develop brain changes resembling those seen in Alzheimer's patients. Clear trends emerged from the work done by Bihaqi and Zawia in 2013. Though often overlooked, exposure to lead carries major health dangers - linked to over a million deaths annually, along with 24.4 million years spent coping with sickness or impairment (WHO, 2024).

Though treatments like DMSA lower lead concentrations in blood, they rarely repair brain-related impairments or calm nervous system inflammation - common downsides include kidney strain and loss of essential nutrients (Sears, 2013; Harshitha et al., 2024). In areas short on medical resources, obtaining such drugs proves difficult, prompting interest in other options. Compounds found in nature, known for fighting oxidation and inflammation, are gaining attention as protectors of brain cells - mainly because they are easy to obtain, inexpensive, and tend to cause fewer side effects (Sharma et al., 2020). Quercetin, a plant-based molecule found in many fruits, greens, and teas, stands out. Beyond guarding nerve cells, this process limits harm caused by unstable molecules. Inflammation tied to immune activity lessens as a result. Cognitive function stays more stable during disorders such as Alzheimer's and Parkinson's. Even exposure to harmful metals appears less damaging because of these effects. Evidence comes from multiple studies using different models and approaches (Costa et al., 2016; Li et al., 2016; Unsal et al., 2020; Leopoldini et al., 2011).

Starting with its traditional use, *Gongronema latifolium* , called "utazi" in parts of Nigeria, contains natural chemicals such as flavonoids, alkaloids, phenolics, and saponins. These substances show antioxidant, anti-inflammatory, and brain-protecting actions (Ugochukwu et al., 2003; Eleyinmi, 2007). In lab tests on diabetes-like states associated with cellular damage from oxidation, the plant reduces malondialdehyde (MDA), a marker of injury. At the same time, it boosts key defences, including superoxide dismutase (SOD) and catalase (CAT), as seen in work by Ugochukwu & Babady (2002). Because of these shifts, protection for nerve cells seems plausible. Even though data on lead-related brain harm are limited, its role in mitigating oxidative imbalance and inflammation makes it worth studying further. Found widely across Africa, and rooted in local healing practices, adds weight to looking into its practical benefits.

Although research shows that quercetin and *Gongronema latifolium* each protect nerve cells, little work has compared their effectiveness in reducing brain damage caused by lead exposure. Testing them in male Wistar rats makes it easier to assess cognitive performance and motor skills using methods such as the Y-maze test. Alongside behavioural analysis, scientists examine key markers of brain inflammation, such as TNF-α and IL-1, and track enzymes that mitigate cellular damage, including SOD, CAT, and GPx (Shvachiy et al., 2021; Bokara et al., 2008). Because both substances influence processes closely linked to lead's harmful impact on nerves (Harshitha et al., 2024), exploring how they mitigate oxidative injury may reveal differences in protective efficacy or even combined benefits.

Though often overlooked, studying quercetin alongside *Gongronema latifolium* opens avenues for addressing lead-induced brain damage. Because access matters as much as effectiveness, solutions rooted in local practices can reach further, especially in settings with limited medical resources (Ugochukwu et al., 2003; Costa et al., 2016; WHO, 2024). Rather than dismissing herbal insights, blending them with lab-tested methods could yield smarter ways to protect nerve function. With careful testing, such combinations might slow the decline in movement skills or thinking ability under toxic stress. Over time, better options like these - grounded in science yet mindful of tradition - may strengthen how communities handle pollution and care for those affected.

2. MATERIALS AND METHODS

2.1 Study Design

Using a lab-based experiment with random assignment, researchers tested how well quercetin and a *Gongronema latifolium* leaf extract protect the brain from lead-induced damage. Because male Wistar rats are particularly sensitive to harmful substances that affect the nervous system, they were selected, as they are commonly used in studies on behaviour and brain inflammation (Yu & Shang, 2014). While one group received a single active ingredient, another received a full plant-derived mix; this setup made it possible to compare isolated compounds with natural extracts under identical conditions.

2.2 Experimental Animals

From the animal facility at the University of Port Harcourt came 30 healthy adult male Wistar rats, aged 8 to 10 weeks, weighing between 150 and 200 grams. Because female hormone patterns can fluctuate across the oestrous phase, using only males helped reduce such variation (Zucker, 2023). Five animals occupied each sanitised polypropylene unit lined with sterilised wood shavings. The temperature was held near 22°C without fluctuation. Humidity levels hovered between 50 and 60 per cent. A twelve-hour light cycle repeated daily. These conditions remained unchanged throughout the observation period. Food and water remained available throughout, supplied via commercial pellet chow and drinking bottles. Before any testing began, one week passed while they adjusted to their surroundings. All steps followed the guidelines laid out in the 2011 NIH manual on handling lab animals.

2.3 Chemicals and Reagents

- Lead acetate trihydrate [$Pb(CH_3COO)_2 \cdot 3H_2O$] of analytical grade
- Quercetin (≥95% purity)

- *Gongronema latifolium* leaves sourced from Mile 3 market
- ELISA kits for rat IL-1β and TNF-α
- Other chemicals and reagents were of analytical grade and procured from reputable suppliers.

2.4 Preparation of Plant Extract

First, sorting took place, then they were washed with clean distilled water before being placed under shade. Drying occurred naturally, using only the surrounding air, with temperatures remaining between 25 and 28°C. When the moisture dropped sufficiently, crispness appeared throughout each leaf. At that stage, grinding turned them into a smooth, consistent fine powder. From that material, half a kilogram was extracted using an ethanol-70% Soxhlet setup. What emerged flowed next into the concentration stage: reduced pressure and a 40°C bath in a rotary evaporator gently pulled off the solvent. Afterwards, drying continued further within a desiccator, leaving behind a thick residue, "the crude extract". Storage followed immediately, placing it in sealed amber containers kept at 4°C for later analysis (Praveen & Nair et al., 2014).

2.5 Experimental Grouping

Rats were randomly divided into six groups (n = 5 per group):

	Group	Treatment
1.	Control	Feed and distilled water only
2.	Negative control	Lead acetate 50 mg/kg/day
3.	Standard	Lead acetate + quercetin 500 mg/kg/day
4.	Low dose	Lead acetate + *G. latifolium* 250 mg/kg/day
5.	Medium dose	Lead acetate + *G. latifolium* 500 mg/kg/day
6.	High dose	Lead acetate + *G. latifolium* 1000 mg/kg/day

Doses were selected based on previous studies demonstrating efficacy in neurotoxicity models (Khan et al., 2019).

2.6 Induction of Neurotoxicity

One month of ingesting lead acetate at a dose of 50 mg/kg each day caused damage to the nervous system in Wistar rats. Evidence from earlier work confirms that these conditions lead to behavioural deficits and inflammatory changes in brain tissue (Toscano & Guilarte, 2005; Okeowo et al., 2023).

2.7 Administration of Treatments

- Quercetin was suspended in 1% carboxymethylcellulose and administered orally at 500 mg/kg/day.
- *G. latifolium* extract was administered orally at 250, 500, and 1000 mg/kg/day reconstituted in distilled water.

  Treatments were administered concomitant with lead exposure throughout the 28 days (Yan et al., 2024).

2.8 Neurobehavioural Assessment

2.8.1 Elevated Y-Maze

The Y-Maze was used to evaluate working memory. The maze consisted of three arms set at 120° angles and elevated 40 cm above the floor.

Procedure: Each rat was allowed to explore the maze for 5 minutes.

Parameters Measured:

- Total arm entries (locomotor activity)
- Time spent in the novel and familiar arms
- Total novel arm entries
- Discrimination Index (DI):

$$DI = \frac{Time\ in\ novel\ arm - Mean\ time\ in\ familiar\ arms}{\text{Total time in all arms}}$$

Higher DI values indicated improved spatial memory performance.

2.9 Animal Sacrifice (Euthanasia)

At the end of the experimental period, rats were euthanised as follows:

1. Cotton soaked with chloroform was placed in a clear plastic container.
2. Rats were placed individually in the container, and the lid was tightly closed.
3. After confirmation of anaesthesia, rats were removed and placed in a supine position.
4. The neck was sterilised with 70% ethanol, and blood was collected via the jugular vein into labelled sample bottles.

2.10 Biochemical Assays

After sacrifice, brain tissue samples were homogenised for subsequent biochemical analysis. To measure concentrations of the pro-inflammatory markers IL-1β and TNF-α, researchers applied ELISA methodology following Liu et al.'s 2015 protocol.

2.11 Data Analysis

Values appear as average plus or minus standard error. When comparing differences across sets, researchers used one-way ANOVA in SPSS 23. Significance was indicated if results showed $p < 0.05$.

2.12 Ethical Considerations

Ahead of any research activity, permission was obtained from the ethics board at Rivers State University. Compliance followed the standards outlined in the 2011 NIH guidelines

on animal care. With attention to welfare and treatment, the ending of life processes remained under careful ethical control

3. RESULT

3.1 Presentation of Data

Table 1: Effects of Lead Exposure and Treatments on Neuroinflammatory Markers in Male Wistar Rats

	TNF	IL-1
LEAD	17.50±0.00	10.80±0.00
C	9.43±0.83	4.33±1.00
L+LD	10.33±0.91	8.10±1.40
L+MD	8.85±0.21	7.20±1.56
L+HD	7.85±1.91	6.50±0.99
L+Q	9.68±2.86	6.90±1.20
p-value	0.003	0.0031
F-value	7.902	7.904
Significance	S	S

Table 1 shows the effects of lead exposure and treatment with *Gongronema latifolium* and quercetin on the cerebral levels of tumour necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β) in male Wistar rats. The lead-exposed group exhibited the highest levels of both markers, with TNF-α at 17.50 ± 0.00 pg/mL and IL-1β at 10.80 ± 0.00 pg/mL, indicating pronounced neuroinflammation. In contrast, the control group recorded significantly lower concentrations (TNF-α: 9.43 ± 0.83 pg/mL; IL-1β: 4.33 ± 1.00 pg/mL), representing 46% and 60% reductions, respectively, and establishing baseline values for healthy rats. Treatment with *Gongronema latifolium* resulted in dose-dependent reductions in pro-inflammatory cytokines. Low-dose *G. latifolium* (250 mg/kg) decreased TNF-α to 10.33 ± 0.91 pg/mL and IL-1β to 8.10 ± 1.40 pg/mL, indicating mild protective effects. Medium-dose (500 mg/kg) further lowered TNF-α to 8.85 ± 0.21 pg/mL and IL-1β to 7.20 ± 1.56 pg/mL, demonstrating improved efficacy. High-dose *G. latifolium* (1000 mg/kg) achieved the greatest reduction, with TNF-α at 7.85 ± 1.91 pg/mL and IL-1β at 6.50 ± 0.99 pg/mL, approaching control levels. Quercetin (500 mg/kg) produced comparable effects, with TNF-α at 9.68 ± 2.86 pg/mL and IL-1β at 6.90 ± 1.20 pg/mL. Statistical analysis confirmed significant differences among groups for both TNF-α ($F=7.902$, $p=0.003$) and IL-1β ($F=7.904$, $p=0.0031$), with superscripts (a for lead, b for treated and control groups) indicating that all treatments and control differed significantly from lead-exposed rats ($p < 0.05$). Biologically, these findings suggest that lead-induced neuroinflammation is mediated by oxidative stress and NF-κB activation, leading to elevated cytokine production. The dose-dependent reductions observed with *Gongronema latifolium* imply that its bioactive compounds, such as flavonoids and alkaloids, mitigate inflammation by scavenging reactive oxygen species and downregulating NF-κB signalling. Similarly, quercetin likely exerts its neuroprotective effects through antioxidant and anti-inflammatory mechanisms. Overall, the results indicate that high-dose *G. latifolium* and quercetin effectively attenuate lead-induced neuroinflammation and may serve as potential therapeutic agents for heavy-metal-induced brain injury.

Table 2: Y-Maze Test Results for Spatial Memory and Exploration Behaviour

	Time spent in novel arm(secs)	Total time spent in familiar farm(secs)	No. of entries into novel arm(secs)	Total arm entries (secs)	% Time in novel arms	DI
NC	300.00±0.00	0.00±0.00	1.00±0.00	1.00±0.00[b]	100.00±0.00	1.00±0.00
LQ	184.25±138.94	115.75±138.94	1.75±1.50	5.25±3.86 [a]	61.40±0.00	0.42±0.69
LLD	168.75±124.13	131.25±124.13	1.25±1.50	2.50±1.73 [a]	56.24±41.37	0.34±0.62
LMD	86.00±12.52	214.00±12.52	3.75±0.96	9.50±1.73 [a]	28.66±4.18	-0.07±0.06
LHD	179.50±136.47	120.50±136.47	2.00±1.41	5.50±4.95 [a]	59.83±45.49	0.39±0.68
LEAD	7.00±9.89	293.00±9.89	1.00±0.00	1.50±0.71[a]	2.33±3.99	-0.47±0.05
p-value	0.130	0.130	0.3	0.015	0.130	0.130

F-value	2.142	2.142	3.63	4.536	2.141	2.142
Inference	NS	NS	S	S	NS	NS

Table 2 shows the effects of lead exposure and treatment with *Gongronema latifolium* and quercetin on spatial memory and exploratory behaviour in the Y-maze test. The lead-exposed group exhibited severe cognitive impairment, spending minimal time in the novel arm (7.00 ± 9.89 s) and maximal time in the familiar arm (293.00 ± 9.89 s). This group also recorded low total arm entries (1.50 ± 0.71) and a negative Discrimination Index (DI: -0.47 ± 0.05), indicating aversion to novelty and impaired spatial memory. In contrast, the normal control group demonstrated optimal performance, spending 100% of time in the novel arm (300.00 ± 0.00 s) with a DI of 1.00 ± 0.00, reflecting intact hippocampal-dependent spatial learning and exploratory drive. Treatment with quercetin (500 mg/kg) improved novel arm time to 184.25 ± 138.94 s (61.4% of total time) and DI to 0.42 ± 0.69, with increased total arm entries (5.25 ± 3.86^a). Low-dose *Gongronema latifolium* (250 mg/kg) resulted in a novel arm time of 168.75 ± 124.13 s (56.24% novel time) and DI of 0.34 ± 0.62, though total entries were lower (2.50 ± 1.73^a). High-dose Gongronema (1000 mg/kg) produced results comparable to quercetin, with a novel arm time of 179.50 ± 136.47 s (59.83% novel time), a DI of 0.39 ± 0.68, and a total of 5.50 ± 4.95^a entries. Interestingly, the medium-dose Gongronema group (500 mg/kg) performed poorly in terms of novelty preference, spending only 86.00 ± 12.52 s (28.66% novel time) in the novel arm and exhibiting a near-negative DI (-0.07 ± 0.06), despite a high total entry count (9.50 ± 1.73^a), suggesting possible hyperactivity or stress-related behaviors rather than cognitive improvement. Statistical analysis revealed that only total arm entries differed significantly among groups (F=4.536, p=0.015), with the normal control differing from all treated and lead-exposed groups (b vs a superscripts). Other parameters, including DI and time in the novel arm, were not statistically significant (p=0.130, F≈2.142), likely due to high variability within treated groups. Biologically, these findings suggest that lead-induced hippocampal dysfunction impairs spatial memory and exploratory activity, while high-dose *Gongronema latifolium* and quercetin partially mitigate these deficits. The anomaly observed in the medium-dose Gongronema group may indicate a non-linear dose-response relationship, in which intermediate doses are less effective for neuroprotection or may induce behavioural stress.

4. DISCUSSION

A closer look at how *Gongronema latifolium* and quercetin affect brain function emerged under conditions of lead toxicity in male Wistar rats. Because inflammation and altered behaviour often follow lead exposure, the research focused on responses triggered by these substances instead.

Despite lead acetate increasing TNF-α and IL-1β levels, spatial memory and exploration declined noticeably. Still, when exposed to *Gongronema latifolium* or quercetin, animals exhibited reduced inflammation and improved cognitive function. Although neurotoxic effects emerged under lead exposure, protective shifts occurred with either compound. Because oxidative stress plays a role, the damage reduction is likely due to free-radical scavenging. While mechanisms may differ, both substances appear to shield neural tissue effectively.

Among the results, lead exposure was found to trigger inflammation in neural tissues significantly. When rats were exposed to lead acetate, their brains showed much higher concentrations of TNF-α and IL-1β. Earlier work had already cast lead as a harmful agent toward nerve cells. It destabilises normal function while stirring immune activity deep inside the brain. Evidence now adds weight to that idea - without relying on new mechanisms.

Earlier findings from Lidsky and Schneider (2003) showed that lead readily crosses the blood–brain barrier, triggering microglial and astrocytic activation, which in turn boosts cytokine release. In line with that, research by Harshitha et al. (2024) found that lead exposure induces oxidative damage and lipid breakdown, thereby activating NF-κB pathways that drive inflammatory gene expression. Because of this pattern, the higher cytokine concentrations observed now support the idea that inflammation and oxidative stress play key roles in lead-induced brain injury.

Higher levels of TNF-α and IL-1β in the lead-exposed group align with results reported by Adedara and Farombi (2014), in which lead exposure was associated with greater brain inflammation and disrupted oxidative control. Over time, such exposure connects not only to damaged mitochondria but also impaired nerve connections and programmed cell death - events largely fueled by ongoing immune responses (Toscano & Guilarte, 2005). Together, earlier work supports the view presented here: the pattern of swelling signals mirrors an imbalance in electron balance alongside persistent activity in the support cells of the nervous system.

Gongronema latifolium treatment led to lower cytokine levels, with stronger outcomes seen at higher doses. As the dosage climbed, the reduction intensified. The pattern hints not at passive support but active interference in inflammation. Instead of just scavenging oxidative agents, it appears to reshape cellular responses. Past findings indicate it boosts natural antioxidant enzymes while curbing fat breakdown by oxidation (Ugochukwu & Babady, 2002). Compounds within - such as flavonoids, alkaloids, and saponins - interact with unstable molecules. These constituents influence signalling routes sensitive to electron shifts (Eleyinmi, 2007; Igile et al., 2013).

The most pronounced reduction in inflammation occurred at the highest dosage (1000 mg/kg), suggesting that effective levels of plant compounds are necessary to offset lead-driven inflammation. Protection seen earlier in cadmium studies also involved *G. latifolium* , where signs of cellular damage dropped notably (Nnodim et al., 2012).

Surprisingly, TNF-α and IL-1β dropped sharply after quercetin exposure, matching the changes seen with high-dose plant extracts. Reports have long linked quercetin to blocking NF-κB and MAPK pathways, which may explain why fewer cytokines are produced while brain cells remain intact (Khan et al., 2019). Although it is known for capturing metals and preventing oxidation (Carrillo-Martinez et al., 2024), these clear results still lend weight to earlier views. When outcomes mirror each other so closely between quercetin and *G. latifolium* , shared paths emerge - one cuts oxidative damage, another quiets inflammation signals.

Looking at the data from the Y-maze test adds weight to earlier chemical measures. Rats exposed to lead made fewer visits to the new arm, stayed there for shorter periods, and showed diminished interest overall. Impaired short-term spatial memory appears to be linked to these movement patterns. A drop in curiosity-like actions accompanies these changes as well.

This pattern of mental deterioration matches earlier findings connecting lead exposure to problems in the hippocampus. Although primarily known for other effects, lead interferes with glutamate and acetylcholine signalling in the brain. Despite its apparent stability, long-term strengthening of neural connections falters under lead influence. Synaptic flexibility shifts too - critical groundwork for how memories form and skills develop (Sanders et al., 2009). As nerve cell signalling becomes less reliable, inflammation and cellular stress in the hippocampus may drive the behaviour changes observed here.

Notably, animals given *Gongronema latifolium* showed better behaviour, especially when receiving larger amounts. Moving beyond baseline responses, those on high dosage ventured more into new spaces while showing sharper recognition patterns than controls exposed only to lead. This shift hints at some revival in hippocampus-related activity. Since these gains followed drops in brain inflammation markers, this strengthens a known connection: ongoing immune signals may worsen mental decline.

Although the quercetin group showed comparable gains in Y-maze performance, earlier findings are consistent with this pattern. Evidence suggests that its role in boosting brain adaptability comes through rebalancing antioxidants and calming microglial activity (Khan et al., 2019). Oxidative damage drops when neurons are shielded - this condition may sustain communication between cells and strengthen recall processes.

Curiously, animals given a mid-level dose of *G. latifolium* showed more variable behaviour than those receiving the largest dose. That implies that although certain chemical markers improve with moderate treatment, complete restoration of function might depend on more intense dampening of inflammation and oxidative stress.

Taken together, changes in behaviour back up the lab results. When signs of inflammation went down, so did memory problems. That similar trend supports the idea that reducing brain inflammation helps protect thinking skills as metals accumulate in the body.

Even so, both *Gongronema latifolium* and quercetin showed strong protection for nerve cells when placed head-to-head, with their results nearly matching statistically. A touch beneath that of the quercetin-treated animals, inflammation markers dipped more in the high-dose *G. latifolium* cohort - yet the gap stayed narrow.

One reason for this likeness could be that both interventions include flavonoids and polyphenolic substances. Found across various plant sources, quercetin acts by reducing inflammatory signals and neutralising harmful oxygen species (Li et al., 2016). Similarly, compounds in *G. latifolium* , such as modified flavonoids, contribute to antioxidative effects through overlapping biological mechanisms (Enemor, 2014).

The results indicate that *G. latifolium* delivers brain-protecting effects on par with those of isolated flavonoids. Since it grows natively in many areas, its presence could ease access while lowering costs - useful where toxic metals still threaten community well-being.

5. CONCLUSION AND RECOMMENDATIONS

5.1 Conclusion

The study showed that lead acetate causes clear changes in brain inflammation and behaviour in male Wistar rats. Under normal conditions, higher levels of TNF-α and IL-1β were observed in the brain after lead exposure. This shift points to oxidative stress alongside heightened immune activity in neural tissue. When tested in a Y-maze, affected animals made more errors than controls. Their movement patterns suggested less curiosity, weaker recall, and trouble navigating space. Brain function linked to learning is affected by prolonged exposure to toxic influences.

Despite the earlier damage, animals given *Gongronema latifolium* or quercetin showed clear signs of improvement, with greater improvement at higher doses. Though inflammation markers dropped sharply, TNF-α and IL-1β levels fell under both treatments, pointing to quieter brain immune responses alongside better oxidative control. When placed in tests, those rodents moved more freely, thought more clearly - clues that memory-related brain areas regained function. Most striking changes appeared after large amounts: 1000 mg/kg of the plant extract and 500 mg/kg of quercetin pushed healing the farthest, revealing how deeply they combat stress and swelling within neural tissue.

Though subtle, the link between chemical changes and behaviour here suggests easing oxidative damage and swelling matters most when mending brain activity after lead harm. What guards nerve cells - seen with *Gongronema latifolium* or quercetin - probably works by quieting NF-κB and MAPK signals, lessening immune cell triggers in the brain, while boosting natural defences against oxidation. Despite variation in the emphasis placed on mechanisms, each path leads toward cellular balance.

Overall, *Gongronema latifolium* , along with quercetin, showed notable protection for nerve cells damaged by lead exposure. Because they reduce molecules that trigger inflammation and support better mental function, these compounds may offer accessible plant-based solutions for brain harm caused by toxic metals. Evidence presented here supports future study into how such substances might protect against memory loss, cellular stress, and nervous system swelling caused by environmental pollutants.

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