

Research Article**Effect of Sacha Inchi Oil on Malondialdehyde and Clinical Parameters in Chlorpyrifos-Exposed Rats*****Pengaruh Minyak Sacha Inchi terhadap Malondialdehida dan Parameter Klinis Tikus Terpapar Klorpirifos*****Putri Rahayu, Tatang Tajudin*, Yuniariana Pertiwi**

Department of Pharmacy, Faculty of Pharmacy Science and Technology, Universitas Al-Irsyad Cilacap, Cilacap, 53223, Central Java, Indonesia

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April 30, 2026*Corresponding Author:
tatang.tajudin@yahoo.co.idCopyright
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4.0 license.**ABSTRACT**

The use of chlorpyrifos remains prevalent in Indonesia, and excessive exposure can trigger oxidative stress, as indicated by increased Malondialdehyde (MDA) levels. Sacha inchi oil (*Plukenetia volubilis* L.) contains antioxidant compounds that may mitigate oxidative stress. This study investigated the effect of sacha inchi oil on plasma MDA concentrations, Body Weight (BW), and clinical parameters in male Wistar rats exposed to chlorpyrifos. Thirty rats were allocated to five groups (n=6 per group): a normal control, a negative control receiving chlorpyrifos 10 mg/kg BW/day, and three treatment groups receiving sacha inchi oil orally at doses of 1, 2, and 4 mL/kg BW/day for 28 days. Plasma MDA levels were measured using the Thiobarbituric Acid Reactive Substances (TBARS) method with spectrophotometric detection at 532 nm, and data were analysed by One-Way ANOVA followed by Tukey's HSD test. Chlorpyrifos exposure increased MDA levels (18.83 nmol/mL) compared with the normal control, whereas sacha inchi oil reduced MDA levels in a dose-dependent manner to 11.32, 8.98, and 3.90 nmol/mL (p<0.05). Supplementation promoted BW gain and ameliorated clinical manifestations, including lethargy, alopecia, and increased respiratory rate, with no mortality observed in treated groups. Sacha inchi oil exhibited protective effects against chlorpyrifos-induced oxidative stress, demonstrating maximal efficacy at 4 mL/kg BW/day.

Keywords: Antioxidants; Chlorpyrifos; MDA; Oxidative Stress; *Plukenetia volubilis* L.**ABSTRAK**

Penggunaan pestisida klorpirifos masih dominan di Indonesia, dan penggunaan berlebihan dapat memicu stres oksidatif, yang ditunjukkan oleh peningkatan kadar malondialdehida (MDA). Minyak sacha inchi (*Plukenetia volubilis* L.) mengandung senyawa antioksidan yang dapat mengurangi stres oksidatif. Penelitian ini menyelidiki pengaruh minyak sacha inchi terhadap konsentrasi MDA plasma, Berat Badan (BB), dan parameter klinis pada tikus Wistar jantan yang terpapar klorpirifos. Tiga puluh tikus dibagi menjadi lima kelompok (n=6 per kelompok): kelompok kontrol normal, kelompok kontrol negatif yang menerima klorpirifos 10 mg/kg BB/hari, dan tiga kelompok perlakuan yang diberikan minyak sacha

inchi secara oral dengan dosis 1, 2, dan 4 mL/kgBB/hari selama 28 hari. Kadar MDA plasma diukur dengan metode Thiobarbituric Acid Reactive Substances (TBARS) dengan deteksi spektrofotometri pada 532 nm, dan data dianalisis dengan ANOVA satu arah diikuti dengan uji HSD Tukey. Paparan klorpirifos meningkatkan kadar MDA (18,83 nmol/mL) dibandingkan dengan kontrol normal, sedangkan minyak sachai inchi menurunkannya secara bergantung dosis menjadi 11,32, 8,98, dan 3,90 nmol/mL ($p < 0,05$). Suplementasi meningkatkan pertambahan BB dan memperbaiki manifestasi klinis, termasuk lesu, kerontokan rambut, dan peningkatan laju pernapasan, tanpa kematian pada kelompok yang diberi perlakuan. Minyak sachai inchi menunjukkan efek perlindungan terhadap stres oksidatif yang diinduksi klorpirifos, menunjukkan efikasi maksimal pada 4 mL/kg BB/hari.

Kata Kunci: Antioksidan; Klorpirifos; MDA; *Plukenetia volubilis* L.; Stres Oksidatif

INTRODUCTION

The use of pesticides has become a major issue in modern agriculture, particularly in developing countries such as Indonesia. A recent case of pesticide residues exceeding permissible limits in Shine Muscat grapes in Thailand has drawn international attention, leading Indonesia to conduct a comprehensive analysis of similar samples (1). The analysis confirmed that residues, including chlorpyrifos, remained within permissible limits; however, this underscores the need for continuous monitoring given the potential risks of long-term exposure. The agricultural sector, which employs more than 40 million workers (2), remains highly vulnerable to pesticide hazards, especially as a result of excessive and non-standardised practices. The World Health Organization reported 1–5 million pesticide poisoning cases each year, with approximately 220,000 deaths, while in Indonesia, 190 cases in males and 144 cases in females were recorded in 2020 (3,4).

Chlorpyrifos, an organophosphate insecticide, is one of the most widely used pesticides globally and is estimated to account for 40% of total insecticide applications (5). Intensive use, such as twice-weekly spraying reported by Pramhesti *et al.*, (2024) (6), increases the risk of residue accumulation in the environment and biological systems. Its main toxic mechanism involves inhibition of Acetylcholinesterase (AChE), along with stimulation of free radical formation, which promotes lipid peroxidation and cellular damage (7). Several studies have associated organophosphate exposure with increased oxidative stress and the risk of degenerative diseases. Oxidative stress develops when Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) exceed the capacity of the endogenous antioxidant system. Elevated Malondialdehyde (MDA) concentrations, a lipid peroxidation product, are widely used as a biomarker of oxidative stress and cellular damage (8).

Exogenous antioxidants from natural sources are crucial when endogenous defences are inadequate. Bioactive compounds such as flavonoids, vitamin E, α -tocopherol, and provitamin A have been proven effective in neutralising free radicals with fewer side effects compared with synthetic antioxidants. The seed oil of sachai inchi (*Plukenetia volubilis* L.) is considered a potential natural oxidation-inhibiting agent, owing to its composition of omega-3 and omega-6 fatty acids, vitamins A, D, and E, as well as polyphenolic constituents. Its antioxidant potential is evidenced by an IC₅₀ value of 8.86 ppm in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay (9,10), and it has shown the ability to reduce oxidative stress in various animal models, including models of hyperglycaemia and epilepsy (11–13).

Studies on the antioxidant effects of sachai inchi oil against chlorpyrifos-induced oxidative stress remain limited, particularly in experimental models relevant to occupational and agricultural exposure in Indonesia. Chronic chlorpyrifos exposure among farmers continues to represent a public health concern, while locally accessible, evidence-based nutraceutical preventive strategies remain scarce. This study provides additional in vivo evidence that sachai inchi oil, as a natural antioxidant option, may

attenuate oxidative stress, as reflected by plasma MDA levels in Wistar rats, thereby addressing a local experimental gap relevant to occupational health surveillance and future translational nutritional research.

MATERIALS AND METHODS

Materials

Sacha inchi oil was obtained from PT Moringa Fangardana Indonesia with a certificate of analysis number SIG.LHP.IX.2023.12155609. Chlorpyrifos (Topban 400 EC®, 400 g/L, Dow AgroSciences, Indonesia) was used. Additional reagents included glacial acetic acid (Merck®), trichloroacetic acid (Merck®, Germany), thiobarbituric acid (Merck®, Germany), sterile aqua pro injection (OTSU-WI®, Indonesia), and distilled water. The experimental animals comprised 30 male Wistar rats (*Rattus norvegicus*), aged 8–10 weeks and weighing 150–200 g. The animals were obtained from a licensed local breeder (Iman Saiman, Banyumas, Central Java, Indonesia).

Methods

Male Wistar rats (*Rattus norvegicus*) were employed in this study following approval from the Research Ethics Committee of Universitas Muhammadiyah Purwokerto, Indonesia, under registration number KEPK/UMP/275/I/2025.

Animal Acclimatisation

The rats weighed 150–200 g and were allowed a seven-day acclimatisation period under standard laboratory conditions, maintained at 22–25°C, 55–65% relative humidity, and a 12-hour light/dark cycle. Rats were provided with standard pellet feed (15–20 g/rat/day) and water *ad libitum*. After acclimatization, the animals were randomly divided into five experimental groups. During the study, Body Weight (BW) was monitored daily using an animal weighing scale to determine the pattern of BW changes.

Treatment and Induction

Sacha inchi oil was administered orally at doses of 1, 2, and 4 mL/kg BW/day for 28 consecutive days. Administration was conducted 30 minutes prior to chlorpyrifos induction. Chlorpyrifos was administered orally at a dose of 10 mg/kg BW/day for 28 days, following the method described by Lal *et al.*, (2022) (14). The chlorpyrifos solution was prepared by diluting 3 mL of Topban 400 EC® in distilled water to a final volume of 120 mL. The dosing volume was measured using a measuring cylinder (Pyrex®) and prepared in a beaker (Pyrex®), with a glass rod used for mixing.

The experimental animals were randomly divided into five groups according to the treatment protocol as follows: the normal control group (normal conditions without treatment or induction); the negative control group (chlorpyrifos 10 mg/kg BW/day); group I (sacha inchi oil 1 mL/kg BW/day); group II (sacha inchi oil 2 mL/kg BW/day); and group III (sacha inchi oil 4 mL/kg BW/day).

Collection of Blood Samples and Preparation of Plasma

Blood was collected from the lateral tail vein on day 36 after a 12-hour fasting period using 3 mL disposable syringes (OneMed®). Samples were collected in K₃-EDTA tubes (Vaculab®, Indonesia) and centrifuged at 3,000 rpm for 15 minutes. Plasma was separated into serum tubes and stored in a cooler bag until analysis.

Determination of Plasma MDA Levels

Plasma MDA levels were measured using the Thiobarbituric Acid Reactive Substances (TBARS) method (15). 1,000 µL of plasma was added with 1 mL of 1% thiobarbituric acid and 2 mL of 20% trichloroacetic acid. The mixture was vortexed and incubated in a water bath (B-One®, China) at 95°C for 45 minutes. After incubation, samples were centrifuged at 3,000 rpm for 15 minutes, and the absorbance of the supernatant was measured at 532 nm using a UV–Vis spectrophotometer (B-One®, China).

Data Analysis

MDA concentrations were determined based on a linear regression equation as described by Mentari and Raihana (2024) (15). IBM SPSS Statistics version 25 (IBM Corporation, USA) was employed for statistical analysis. The data were analysed by One-Way ANOVA, and post hoc comparisons were conducted using Tukey's HSD test. A significance threshold of $p < 0.05$ was applied.

RESULTS

Physicochemical Properties and Fatty Acid Profile of Sacha Inchi Oil

The physicochemical properties and fatty acid profile of the sacha inchi oil used in this study are summarised in **Table 1** and **Table 2**. The results confirm that the oil's quality aligns with the standards specified in the Certificate of Analysis (COA).

Table 1. Physicochemical Characteristics of Sacha Inchi Oil

Parameter	Result
Moisture Content (%)	0.06
Ash Content (%)	<0.02
Total Fat (%)	99.94
Protein (%)	<0.04
Carbohydrate (%)	0
Vitamin A ($\mu\text{g}/100\text{ g}$)	64.27
Vitamin E ($\text{mg}/100\text{ g}$)	0.74

The fatty acid profile of the sacha inchi oil used in this study is presented in **Table 2**. These findings illustrate the predominance of unsaturated fatty acids, particularly omega-3 and omega-6, which are recognised for their significant roles in antioxidant mechanisms and pharmacological potential.

Table 2. Fatty Acid Composition of Sacha Inchi Oil

Component	Result (%)
α -Linolenic Acid (ω -3)	49.09
Linoleic Acid (ω -6)	36.94
Oleic Acid (ω -9)	7.81
Palmitic Acid (C16:0)	2.90
Stearic Acid (C18:0)	2.77
Heptadecanoic Acid (C17:0)	0.08
Arachidic Acid (C20:0)	0.09
Eicosenoic Acid (C20:1)	0.25
Total Saturated Fatty Acids	5.85
Total Unsaturated Fatty Acids	94.09
Polyunsaturated Fatty Acids	86.03
Monounsaturated Fatty Acids	8.06
Total Omega-3	49.09
Total Omega-6	36.94
Total Omega-9	7.81

Measurement of MDA Levels

The absorbance values obtained from the TBARS assay at 532 nm were converted into MDA concentrations by adopting the validated standard curve equation ($y = 0.0184x + 0.1241$) from the reference study (15). This established equation was used under identical analytical conditions, thereby allowing the present study to focus on the pharmacological impact of sacha inchi oil in Wistar rats. The resulting MDA levels for each experimental group are summarised in **Table 3**.

Table 3. Plasma MDA Levels of Wistar Rats under Different Treatments

Treatment Group	Mean±SD MDA Concentration (nmol/mL)
Normal Control Group	10.91±2.38 ^{b,e}
Negative Control Group	18.83±3.35 ^{a,c,d,e}
Group I	11.32±3.66 ^{b,e}
Group II	8.98±2.96 ^b
Group III	3.90±3.68 ^{a,b,c}

Notes: ^a= significantly different from group normal control; ^b= significantly different from group negative control; ^c= significantly different from group I; ^d= significantly different from group II; ^e= significantly different from group III

The results in **Table 3** demonstrate significant differences among the experimental groups. The chlorpyrifos-exposed negative control group showed the highest plasma MDA levels, indicating severe oxidative stress. By contrast, the normal control group without any treatment demonstrated considerably lower MDA levels, representing normal physiological conditions in the absence of toxicant exposure. The treatment groups revealed a marked reduction in MDA levels following administration of sachai inchi oil. A clear dose-dependent pattern was observed, whereby Group I showed a modest decrease, Group II displayed a greater reduction, and Group III (4 mL/kg BW/day) recorded the lowest MDA concentration, indicating a dose-dependent reduction in lipid peroxidation and attenuation of chlorpyrifos-induced oxidative stress. Overall, these findings indicate that sachai inchi oil effectively reduces plasma MDA levels in a dose-dependent manner. The progressive decline across groups highlights the potential of higher doses not only to counteract oxidative stress but also to restore biochemical balance towards physiological levels. This supports the beneficial role of sachai inchi oil as a natural antioxidant in protecting against chlorpyrifos-induced oxidative stress.

Pattern of Body Weight (BW) Changes with Treatment

This analysis provides an overview of the relationship between treatment factors and the physiological changes observed in the experimental subjects. The descriptive pattern of weekly BW changes among the experimental rats over the four-week observation period is illustrated in **Figure 1**.

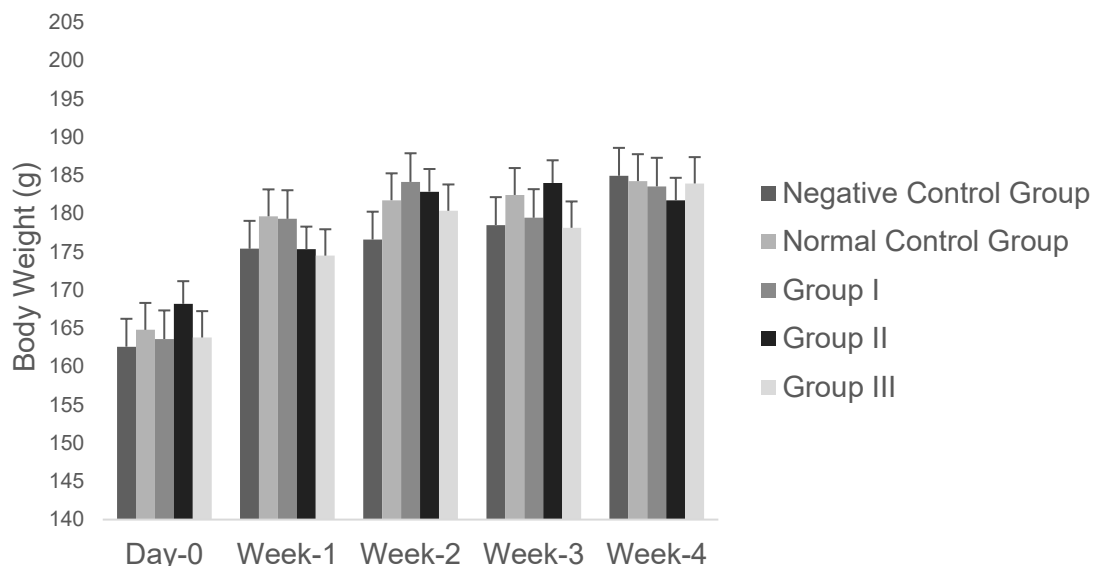


Figure 1. The effect of sachai inchi oil administration on BW changes in the negative control group, normal control group, and treatment groups (Groups I, II, and III) was measured on day 0 and recorded weekly up to week 4

The data presented in **Figure 1** were recorded from day 0 through week 4 of treatment. The normal control group maintained a relatively stable trajectory of weight gain, although a slight reduction

was observed after the second week. In contrast, the negative control group exhibited a slower rate of weight gain and consistently remained at a lower BW compared with the other groups. The treatment groups displayed distinct patterns of weight change. Among them, Group III (sacha inchi oil at 4 mL/kg BW/day) showed the most consistent and progressive increase in BW, suggesting sustained improvement throughout the study period. Groups I and II also showed increases, though these were more moderate. Collectively, these findings indicate that the administration of sacha inchi oil was associated with a positive influence on BW, with a dose-dependent trend, under conditions of oxidative stress.

Clinical Signs and Mortality

The effects of the treatments on clinical signs and mortality were assessed, including lethargy, piloerection, and respiratory rate. Mortality and qualitative clinical observations are summarised in Table 4.

Table 4. Mortality and Clinical Signs in Wistar Rats

Parameters	Group				
	Normal Control Group	Negative Control Group	Group I	Group II	Group III
Sample Size	6	6	6	6	6
Mortality	0	1	0	0	0
Clinical Signs					
Decreased Activity	+	+++	++	+	+
Alopecia	+	+++	++	++	++
Respiratory Rate	+	++	+	+	+

Notes: + (Normal); ++ (Mild); +++ (Moderate); ++++ (Severe)

Table 4 summarises the mortality and clinical signs observed in Wistar rats, including mobility/activity, alopecia, and respiration, across the normal control, negative control, and treatment groups (Groups I, II, and III). A single mortality was recorded in the negative control group, indicating that, in the absence of sacha inchi oil intervention, chlorpyrifos exposure exerted a significant toxic effect on the physiological condition of the rats. Clinically, the negative control group exhibited the highest severity, with mobility and activity classified as moderate (+++), characterised by impaired movement and apparent lameness, although the animals were still able to access food and water. Alopecia was also observed at a similar severity. In addition, respiration was categorised as mild (++), indicated by increased respiratory effort visible in the thoracic region. In contrast, the treatment groups, particularly Groups II and III, demonstrated marked improvement, with mobility returning to near-normal conditions, mild improvement in alopecia, and respiration restored to normal, with no mortality observed. Overall, the administration of sacha inchi oil reduced the severity of clinical signs in chlorpyrifos-induced rats, likely due to its antioxidant properties that attenuate oxidative stress, thereby reducing MDA levels and improving physiological status. The classification of clinical severity in this study was based on the guidelines provided by the University Animal Care Committee (2025) (16).

DISCUSSION

The physicochemical characteristics of sacha inchi oil demonstrated very low moisture content (0.06%) and ash content (<0.02%), with an almost pure fat content (99.94%). These parameters indicate high stability and purity, thereby confirming the suitability of this oil for pharmacological studies. The presence of vitamin A (64.27 µg/100 g) and vitamin E (0.74 mg/100 g) further enhances the pharmacological value of the oil, contributing to its antioxidant and immunoprotective properties.

The fatty acid composition revealed that sacha inchi oil is predominantly composed of polyunsaturated fatty acids (PUFAs, 86.03%), mainly α-linolenic acid (omega-3, 49.09%) and linoleic acid (omega-6, 36.94%), with relatively low levels of saturated fatty acids (5.85%). These findings are consistent with previous reports that highlight sacha inchi oil as a valuable source of omega-3, omega-6, and omega-9 fatty acids, with strong antioxidant and anti-inflammatory properties (11). High levels of omega-3 fatty acids and vitamin E act synergistically to reduce lipid peroxidation and MDA

production, thereby supporting the observed protective effect against chlorpyrifos-induced oxidative stress.

The results observed in the chlorpyrifos-exposed negative control group indicate a substantial failure of the body's endogenous antioxidant defence mechanisms to counteract excessive free radical production. This is reflected in significantly elevated MDA levels compared with the normal control group, confirming that chlorpyrifos induces marked oxidative stress. These findings align with previous studies by Khayal and Ahmed (2019) (17), who similarly reported increased lipid peroxidation following chlorpyrifos exposure, underscoring the consistency of oxidative biomarkers across different experimental models. Treatment with sachai inchi oil demonstrated a clear dose-dependent protective effect. Previous literature has documented that doses of 1 mL/kg BW/day can moderately reduce MDA levels, supporting the established antioxidant potential of sachai inchi oil. In this study, higher doses (1, 2, and 4 mL/kg BW/day) were employed to further characterise the dose–response relationship. The 2 mL/kg BW/day dose produced a more substantial reduction in MDA, while the highest dose (4 mL/kg BW/day) yielded the most pronounced decrease, indicating a strong association between dose and protective efficacy. This protective effect can be explained by the high content of polyunsaturated fatty acids in sachai inchi oil, particularly α -linolenic acid (omega-3) and linoleic acid (omega-6), which function as precursors of antioxidant mediators and may stimulate the expression of endogenous antioxidant enzymes, such as Superoxide Dismutase (SOD) and Glutathione (GSH). Additionally, phenolic compounds in sachai inchi oil act as free-radical scavengers that directly inhibit lipid peroxidation. These mechanisms support the observed dose-dependent improvement in oxidative status, as also reported by Sayuti and Yenrina (2015) (18). The dose-dependent trend observed in this study highlights the potential of sachai inchi oil not only to counteract chlorpyrifos-induced oxidative stress but also to confer broader cytoprotective effects against toxins that generate free radicals. The reduction in MDA levels indicates decreased lipid peroxidation and cellular damage, confirming that higher doses of sachai inchi oil more effectively reinforce endogenous antioxidant defences. These effects may be related to the known antioxidant properties of polyunsaturated fatty acids and phenolic compounds, although the underlying mechanistic pathways were not directly assessed in this study.

BW was monitored from day 0 to week 4 of the treatment period. The normal control group exhibited relatively stable weight gain, with a slight decrease after week 2, likely due to environmental stress or social interactions affecting appetite and metabolic balance (19). The negative control group exposed to chlorpyrifos showed slower weight gain during the initial weeks, although a notable increase occurred by week 4. These findings align with earlier studies indicating that exposure to chlorpyrifos hinders weight gain by inducing gastrointestinal disturbances, oxidative stress, and metabolic impairments (20). The treatment groups displayed more progressive weight gain, particularly Group III, in line with Wongmanee *et al.*, (2024) (12), who found that higher doses of sachai inchi oil led to the greatest improvements in BW. This effect is attributed to the oil's omega-3 fatty acid content, which modulates oxidative stress and inflammation while supporting metabolic health, as well as its antibacterial activity that may promote gastrointestinal recovery. These findings also correspond with clinical recommendations indicating that omega-3 fatty acids enhance appetite and aid the recovery of lean body mass (17,21). Overall, sachai inchi oil, particularly at higher doses, demonstrated potential in supporting BW gain and metabolic recovery in chlorpyrifos-exposed rats.

The clinical signs observed, including an increased respiratory rate, are consistent with organophosphate poisoning, which typically involves neuromuscular disturbances due to acetylcholinesterase inhibition (7). Treatment with sachai inchi oil resulted in notable clinical improvements, with symptoms appearing milder at low doses and relatively minimal at higher doses. This effect can be attributed to the antioxidant properties of sachai inchi oil, which mitigate oxidative stress in the nervous system, thereby reducing neuromuscular damage and inflammation commonly induced by chlorpyrifos exposure. Improvements in activity, coat condition, and respiration were consistent with the biochemical findings, as reflected by a significant reduction in plasma MDA levels (22,23). Sachai inchi oil shows potential as a protective agent against oxidative stress, both preventively before toxin exposure through primary mechanisms and therapeutically after oxidative stress has occurred through secondary and tertiary mechanisms. The primary mechanism involves free radical scavenging, in which compounds such as tocopherols and polyphenols, including flavonoids, donate electrons to halt lipid peroxidation chain reactions (24). Secondary mechanisms include Fe^{2+} chelation, which inhibits the formation of highly reactive hydroxyl radicals (25). The tertiary mechanism is chiefly

regulated by omega-3 fatty acids, notably α -linolenic acid, which may enhance endogenous antioxidant defence systems, including SOD and GSH (21,26).

CONCLUSION

Sacha inchi oil demonstrated a marked ability to reduce plasma MDA concentrations in Wistar rats subjected to chlorpyrifos-induced oxidative stress. The effect was clearly dose-dependent, with the most pronounced reduction achieved at 4 mL/kg BW/day. In addition, administration of the oil appeared to support endogenous antioxidant defences, promote weight recovery, alleviate clinical manifestations of toxicity, and reduce mortality. These findings highlight the potential of sachal inchi oil as a natural protective agent; nevertheless, further studies are required to assess its safety profile, optimal dosage, and possible toxicological effects in humans.

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