

Safety evaluation and chemopreventive potential of licuri (*Syagrus coronata*) oil in a colorectal carcinogenesis rodent model

Nathália Oliveira Acésio, Arthur Barcelos Ribeiro, Marcela de Melo Junqueira, Ana Laura de Azevedo, Leticia Gonçalves Xavier, Renato Luis Tame Parreira, Sérgio Ricardo Ambrósio*, Denise Crispim Tavares*

^aUniversity of Franca, Avenida Dr. Armando Salles Oliveira, 201, 14404-600, Franca, São Paulo, Brazil.

***Corresponding authors:**

Sérgio Ricardo Ambrósio (sergio.ambrosio@unifran.edu.br) and Denise C. Tavares (denisecrispim2001@yahoo.com) University of Franca, Avenida Dr. Armando Salles Oliveira, 201, 14404-600, Franca, São Paulo, Brazil.

Abstract

Colorectal cancer is a leading cause of cancer-related morbidity and mortality worldwide. Chronic inflammation and oxidative stress are key drivers of colorectal carcinogenesis, and dietary interventions with bioactive compounds have emerged as promising strategies for cancer prevention. Licuri (*Syagrus coronata*) oil (LO) is rich in medium-chain and unsaturated fatty acids and exhibits antioxidant, anti-inflammatory, and antimicrobial properties. Given these biological activities, it becomes relevant to investigate its chemopreventive potential. This study evaluated the safety and protective action of LO against colorectal carcinogenesis. Furthermore, considering its popular use in cooking, the potential toxicity induced by subchronic administration of heated LO (HLO) was analyzed. Acute oral toxicity was assessed in female rats following a single oral dose of 2000 mg/kg LO, while subchronic toxicity of HLO was evaluated in male rats administered 250 mg/kg for 28 days. Parameters analyzed included clinical signs, body weight, water consumption, behavioral observations, and histopathological and biochemical markers. Chemopreventive effects were investigated in male rats with chemically induced preneoplastic lesions (aberrant crypt foci, ACF). LO was administered orally at doses of 62.5, 125, and 250 mg/kg, and outcomes included ACF counts, biochemical analyses, body weight, water intake, and behavioral monitoring. LO demonstrated a favorable safety profile, with no clinical, biochemical, or histopathological evidence of systemic toxicity, indicating a low toxic risk. Subchronic administration of HLO also produced no adverse effects. On the other hand, LO significantly reduced ACF formation, with the greatest effect observed at the lowest dose (62.5 mg/kg; 81.48% reduction), without any associated toxicological effects. In conclusion, LO has proven to be a safe natural product with substantial chemopreventive action against early colorectal lesions in rats. The absence of systemic toxicity reinforces its potential for use both in cooking and in dietary or nutraceutical interventions for the prevention of colorectal cancer.

Keywords: Dietary supplement, cooking oil, traditional medicine.

1. Introduction

Colorectal cancer (CRC) remains one of the leading causes of cancer-related morbidity and mortality worldwide. Its pathogenesis is a complex and multifactorial process influenced by both genetic predispositions and modifiable environmental factors, particularly diet and lifestyle (Bardelčíková et al., 2022; Acevedo-León et al., 2023; Roshandel et al., 2024). Increasing evidence indicates that chronic inflammation and oxidative stress are pivotal drivers of colorectal carcinogenesis, contributing to the initiation, promotion, and progression of neoplastic lesions. Consequently, there is growing interest in dietary interventions and functional foods capable of modulating these processes to mitigate cancer risk (George et al., 2021; Shankar G et al., 2022).

Dietary patterns rich in bioactive compounds including fibers, antioxidants, and anti-inflammatory agents, have been consistently associated with a lower risk of colorectal cancer. Plant-derived products, particularly those from native and underutilized species, represent valuable sources of bioactive molecules with potential chemopreventive effects (Bardelčíková et al., 2022; Acevedo-León et al., 2023). In this context, the exploration of edible oils rich in specific fatty acids, phenolic compounds, and micronutrients has gained substantial attention for their roles in modulating oxidative stress, inflammation, and even the gut microbiota factors intimately linked to colorectal cancer development.

Licuri (*Syagrus coronata*), a palm species native to Brazil, stands out as a promising candidate within this framework. Widely distributed across the semi-arid Caatinga and the savanna-like Cerrado biomes, licuri plays a crucial socio-economic role for rural communities in northeastern (Pernambuco, Alagoas, Sergipe, and Bahia) and southeastern (Minas Gerais) Brazil (Antoniassi et al., 2022; Inocêncio et al., 2025). Beyond its economic significance, licuri fruits, particularly almonds, are highly valued for their nutritional richness, being an important source of oil and protein for both human consumption and animal feed (Menezes et al., 2024; Pereira et al., 2025).

The oil extracted from licuri almonds is characterized by a unique lipid composition, predominantly rich in saturated fatty acids such as lauric, myristic, and caprylic acids. The fatty acid profile is modulated by factors like fruit maturation and extraction methods, which in turn influence its physicochemical, nutritional, and functional properties (Barbosa et al., 2024; Menezes et al., 2024; Silva et al., 2024; Pereira et al., 2025; Inocência et al., 2025).

In addition to its nutritional value, licuri oil exhibits a diverse range of biological activities that have been recognized in both traditional medicine and recent scientific studies. Notably, it demonstrates antimicrobial activity against various bacterial strains (Bessa et al., 2016; Santos et al., 2019) and significant antioxidant capacity, attributed to the presence of phenolic compounds and other bioactive constituents capable of scavenging reactive oxygen species (Bauer et al., 2013; Belviso et al., 2013; Amorim et al., 2024). Furthermore, licuri oil displays anti-inflammatory properties, likely through the modulation of key inflammatory mediators (Barbosa et al., 2024) and shows selective cytotoxicity against certain tumor cell lines while maintaining a favorable safety profile (Souza et al., 2021). These properties suggest that licuri oil may contribute to cancer chemoprevention, particularly in colorectal cancer, by simultaneously mitigating oxidative stress, suppressing chronic inflammation, and exerting selective cytotoxic effects on transformed cells.

Therefore, considering its use in local cuisine and traditional medicine, the present study aimed to assess the safety for human health in the use of licuri oil, at room temperature and heated, as well as its chemopreventive effect on colorectal carcinogenesis.

2. Material and methods

2.1 Obtaining and preparation of heated licuri oil

The licuri oil (LO) used in this study was kindly provided by the Cooperativa Produtores e Agroextrativistas Frutos da Terra (Coopefrut), Miguel Calmon, Bahia, Brazil. The physicochemical characterization of this oil is described in Pereira et al. (2025). LO was stored in amber glass bottles,

protected from light to prevent oxidation. A portion of the same batch was heated at 180 °C for 30 minutes in a temperature-controlled oven to simulate domestic cooking conditions. The temperature of 180 °C was chosen considering the compositional similarity between licuri and coconut oils, both rich in saturated medium-chain fatty acids. The smoke point of unrefined coconut oil is reported to be around 177 °C, which was used as a reference for defining thermal treatment (Katragadda et al., 2010). After heating, the oil was allowed to cool naturally to room temperature under ambient conditions.

Comentado [DC1]: Renato verificar

2.2 Animals

Male and female Wistar Hannover rats (*Rattus norvegicus*), aged 8–12 weeks, were obtained from the animal facility of the Ribeirão Preto Campus, University of São Paulo (Brazil). The animals were housed in ventilated polypropylene cages under controlled environmental conditions (temperature 23 ± 2 °C, relative humidity $50 \pm 10\%$, and a 12 h light/dark cycle), with free access to standard chow and water ad libitum. All experimental procedures were reviewed and approved by the Ethics Committee on Animal Use of the University of Franca (approval n° 4108270524). Treatments were initiated after a 1-week acclimation period.

2.3 Acute oral toxicity of licuri oil

The acute oral toxicity of LO was evaluated following OECD Guideline 423 (OECD, 2002). Ten healthy, young, nulliparous, non-pregnant female Wistar Hannover rats were acclimated under standard laboratory conditions and fasted for 12 hours prior to dosing. The animals were randomly divided into two groups of five individuals each: the treatment group received a single oral dose of 2000 mg/kg body weight (b.w.) of LO by gavage (1 mL/animal), while the control group received water. Animals were observed individually during the first 30 minutes after dosing, periodically during the first 24 hours, and daily for 14 days. Clinical signs, mortality, and changes in behavior or activity were recorded. Body weights were measured on days 0 and 14, and the weight variation was calculated as the difference between the final (day 14) and initial body weight. Water consumption was monitored

and recorded throughout the study. At the end of the observation period, animals were anesthetized with sodium thiopental (Thiopentax®, Cristália, Itapira, SP, Brazil; 0.48 mg/kg b.w.; intraperitoneal) for blood collection via cardiac puncture for serum biochemical analyses, including creatinine and alanine aminotransferase (ALT). Following blood collection, animals were euthanized with an overdose of sodium thiopental (840 mg/kg b.w.), and a complete necropsy was performed to assess macroscopic alterations and collect organs for further analysis.

2.4 Subchronic oral toxicity of heated licuri oil

The subchronic oral toxicity of heated licuri oil (HLO) was evaluated in male Wistar rats following daily administration for four consecutive weeks. Animals were randomly divided into two groups (n = 5 per group): a negative control (NC), which received water, and a treatment group, which received HLO at a dose of 250 mg/kg b.w. by oral gavage (0.5 mL/animal/day). This dose is equivalent to the human consumption of one tablespoon (14 g of LO). Body weight was recorded weekly throughout the experimental period, and mean body weight gain was calculated as the difference between the initial and final values. Water intake was monitored daily, and the average consumption was expressed as milliliters per animal per day. At the end of the 28-day treatment, animals were anesthetized with sodium thiopental (0.48 mg/kg b.w.) for blood collection via cardiac puncture. Serum samples were obtained by centrifugation and analyzed for biochemical parameters, including creatinine, ALT and total cholesterol. Blood glucose levels were measured at baseline and on the final day of treatment using a glucometer. Following blood collection, animals were euthanized by an overdose of anesthetic (sodium thiopental, 840 mg/kg b.w.), and the colon was excised for microscopic examination. The aberrant crypt foci (ACF; Bird, 1989) assay was used to assess the carcinogenic potential of consuming HLO. ACF were identified after fixation in 10% formalin and staining with 0.2% methylene blue, according to standard histological protocols. Clinical signs, behavioral changes, and mortality were recorded daily throughout the study.

2.5 Assessment of the effect of licuri oil on chemically induced colon carcinogenesis

The ACF assay was used to evaluate the chemopreventive potential of LO, following Bird (1989). Male Wistar Hannover rats were randomly assigned to experimental groups (n = 5 per group) and treated with LO at doses of 62.5, 125, or 250 mg/kg b.w.. Considering the relationship between saturated fat consumption and the risk of cardiovascular disease, dietary guidelines recommend limiting total saturated fat intake to less than 10 percent of calories per day (2025 Dietary Guidelines Advisory Committee, 2024; Snetselaar et al, 2021). In this sense, this recommendation guided the choice of LO doses to be tested. The average saturated fat intake of rodents that received LO was equivalent to 4% of their total daily energy intake. LO was administered once daily by oral gavage (0.5 mL per animal) for four consecutive weeks (28 days). To induce preneoplastic colon lesions, animals received the carcinogen 1,2-dimethylhydrazine (DMH; Sigma-Aldrich, Burlington, VT, USA) at 40 mg/kg b.w. (0.5 mL per animal), freshly prepared in 1 mM EDTA (Labsynth, Diadema, SP, Brazil), given subcutaneously on days 2, 5, 9, and 12 (four injections in total). Animals not receiving DMH (negative control and LO-only groups) were given subcutaneous injections of 1 mM EDTA on the same schedule.

Throughout the experimental period, body weight and water consumption were monitored three times per week to evaluate the general health and possible systemic effects of the treatments. At the end of the experimental period, the animals were euthanized, and the colons were excised, opened longitudinally, rinsed with physiological saline, and processed for histological examination according to the methodology described by Senedese et al. (2013).

After fixation and staining, the total numbers of ACF and aberrant crypts (AC) were quantified under a light microscope by examining 15 sequential microscopic fields per colon segment. The data obtained were used to determine the frequency and distribution of ACF as an indicator of the chemopreventive efficacy of LO. The percentage reduction in ACF frequency in treated groups compared to the DMH control group was calculated using the following formula:

$$\text{Reduction (\%)} = \left(\frac{\text{Mean ACF in DMH group} - \text{Mean ACF in treated group}}{\text{Mean ACF in DMH group}} \right) * 100$$

At the end of each experimental period, blood samples were collected from all animals via cardiac puncture under anesthesia and centrifuged to obtain serum. Serum levels of creatinine, ALT and total cholesterol were measured using commercial reagent kits: Creatinine, ALT/GTP Liquiform, and Cholesterol Liquiform (Labtest Diagnóstico, Lagoa Santa, MG, Brazil), according to the manufacturer's instructions.

The blood glucose levels of the rodents were measured on the first and last day of treatment. Blood samples from the animals were collected through caudal vein and evaluated using FreeStyle Lite® glucose monitoring device from Abbott, following the manufacturer's instructions.

2.6 Statistical Analysis

Data were statistically analyzed using analysis of variance (ANOVA) for completely randomized experiments, with calculation of the F statistic and its corresponding *p*-value. When significant differences were observed (*p* < 0.05), treatment means were compared using Tukey's post hoc test, and the minimum significant difference was calculated at *p* = 0.05. All analyses were performed using GraphPad Prism software (version 6.0).

3. Results

3.1 Acute oral toxicity of licuri oil

The administration of a single oral dose of 2000 mg/kg of LO did not cause mortality or any evident clinical signs of toxicity in Wistar Hannover rats during the 14-day observation period (**Table 1**). All treated animals showed normal behavior and progressive body weight gain (61.2 ± 4.4 g) compared to the negative control group (62.8 ± 5.0 g), with no statistically significant difference between them. Similarly, mean daily water intake was slightly lower in LO-treated rats (34.5 ± 6.5

mL/day) relative to controls (38.4 ± 7.1 mL/day), but without statistical significance. Serum biochemical parameters also remained within normal physiological ranges. Creatinine levels were similar between groups (0.7 mg/dL in LO-treated rats vs. 0.6 mg/dL in controls), indicating preserved renal function. Likewise, no significant differences were observed in serum ALT levels between the treated (44.4 ± 7.1 U/L) and control (51.5 ± 6.3 U/L) groups compared to controls, confirming the absence of hepatic injury. Macroscopic examination during necropsy revealed no visible alterations in major organs, including the liver, lungs, kidneys, heart, pancreas, and gut. According to the criteria of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS), LO can be classified in category 5 (LD_{50} -median lethal dose > 2000 – 5000 mg/kg b.w.), indicating a low risk of acute oral toxicity.

Table 1. Body weight gain, water consumption, and serum biochemical parameters (creatinine and ALT) observed in the acute oral toxicity assessment of licuri oil.

Parameters	Groups	
	Negative control	2000 mg/kg b.w.
Body weight gain (g)	62.8 ± 5.0	61.2 ± 4.4
Water consumption (mL/day)	38.4 ± 7.1	34.5 ± 6.5
Creatinine (mg/dL)	0.6 ± 0.0	0.7 ± 0.1
ALT (U/L)	51.5 ± 6.3	44.4 ± 7.1

ALT – alanine aminotransferase. Values are expressed as mean $\pm$ standard deviation, $n = 5$. No statistically significant differences were detected between the licuri oil–treated and control groups ($p > 0.05$).

3.2 Toxicological assessment of subchronic exposure to heated licuri oil

No clinical signs of toxicity, behavioral alterations, or mortality were observed in any group during the 28-day treatment period in Wistar Hannover rats (Table 2). Both HLO-treated and control

rats remained active and healthy, exhibiting normal patterns of food and water intake. No statistically significant differences were observed in body weight gain between the two groups, treated and control. Similarly, daily water consumption showed a mild, non-significant reduction in HLO-treated rats (46.5 ± 5.0 mL/day) compared to controls (58.7 ± 9.0 mL/day).

Blood biochemical parameters also remained within normal physiological ranges. Serum creatinine concentrations were unchanged between groups (0.8 mg/dL in HLO vs. 0.8 mg/dL in control), suggesting preserved renal function. Serum ALT level was lower in the HLO group (45.6 ± 5.5 U/L) in relation to negative control group (64.5 U/L), indicating no hepatocellular injury. No statistically significant differences were observed in total cholesterol levels between the HLO (46.5 ± 0.5 mg/dL) and negative control (41.0 ± 7.0 mg/dL) groups. Blood glucose variation from baseline to the end of treatment remained minimal in both groups (+0.4 mg/dL in HLO vs. -0.4 mg/dL in negative control), indicating no alteration in glycemic control.

No ACF was detected in the colon of any animal, confirming the absence of preneoplastic lesions under experimental conditions used. Overall, the results demonstrate that subchronic oral administration of HLO at 250 mg/kg for 28 days did not induce systemic toxicity, metabolic disturbances, or histological abnormalities in the colon in rodents.

Table 2. Parameters evaluated in Wistar rats subjected to treatments with heated licuri oil for four weeks.

Parameters	Groups	
	Negative control	HLO
Body weight gain (g)	133.1 ± 21.2	106.6 ± 11.4
Water consumption (mL/day)	58.7 ± 9.0	46.5 ± 5.0
Creatinine (mg/dL)	0.8 ± 0.0	0.8 ± 0.1
ALT (U/L)	64.5 ± 3.1	45.6 ± 5.5
Cholesterol (mg/dL)	41.0 ± 7.0	46.5 ± 0.5
Blood glucose (mg/dL) ^a	-0.4	0.4
ACF (n)	0	0

HLO - 250 mg/kg b.w. of heated licuri oil, 180 °C; ALT – alanine aminotransferase; ACF - aberrant crypt foci. Values are expressed as mean ± standard deviation, n = 5. No statistically significant differences were detected between the heated licuri oil–treated and control groups ($p < 0.05$). ^aBlood glucose: variation between first and last day of treatment.

3.3 Assessment of the effect of licuri oil on chemically induced colon carcinogenesis

Preneoplastic lesions were observed exclusively in the colons of animals treated with DMH, as illustrated in **Figure 1**, whereas no lesions were detected in animals treated with oil alone, nor in those in the negative control group. Treatment with LO at all tested doses resulted in significant reductions in the frequencies of DMH-induced ACF and AC compared to animals treated with the carcinogen alone. The percentage reduction in ACF was 81.48%, 68.89%, and 51.85% for treatments with doses of 62.5, 125, and 250 mg/kg b.w., respectively, indicating that the chemopreventive effect of LO did not increase with higher doses. The lowest frequencies of preneoplastic lesions were observed in rodents treated with the lowest dose of LO tested, 62.5 mg/kg b.w.. It is noteworthy that the frequencies

of preneoplastic lesions observed in the groups treated with 62.5 and 125 mg/kg b.w. were significantly lower than those obtained in rodents treated with the highest dose, 250 mg/kg b.w.

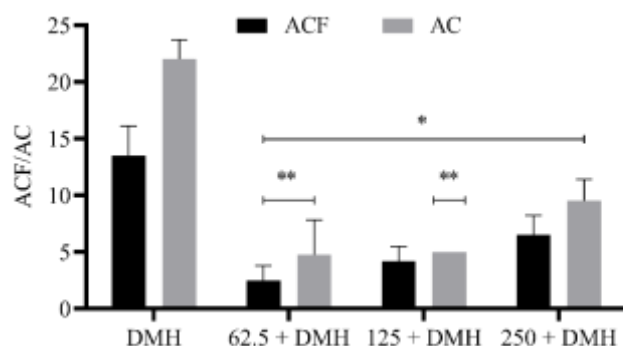


Figure 1. Chemoprevention assessment. Aberrant crypt foci (ACF) and aberrant crypt (AC) observed in the distal colon of Wistar rats treated with licuri oil (62.5, 125 and 250 mg/kg b.w.) plus DMH. DMH - 1,2 Dimethylhydrazine (40 mg/kg b.w.). Values are expressed as mean $\pm$ standard deviation, $n = 5$. *Significantly different of DMH group ($p < 0.05$). **Significantly different of 250 + DMH group ($p < 0.05$).

Considering the toxicity assessment of treatments, **Table 3** presents the data on body weight gain and water intake of the experimental groups. No statistically significant differences were detected in body weight gain among the treated groups when compared to the untreated group. Likewise, water intake remained comparable across all groups, indicating that the treatments did not affect the general health status or hydration behavior of the animals.

Table 3. Body weight gain and water consumption observed in animals treated with licuri oil (62.5, 125 and 250 mg/kg b.w.) plus DMH, and their respective controls.

Groups	Parameters	
	Body weight gain (g)	Water consumption (mL/day)
Negative control	131.1 ± 15.4	58.7 ± 9.0
250	118.4 ± 13.1	49.5 ± 7.4
DMH	117.2 ± 21.9	49.6 ± 11.0
62.5 + DMH	107.4 ± 6.9	49.5 ± 9.1
125 + DMH	101.8 ± 9.4	53.5 ± 8.7
250 + DMH	106.0 ± 19.9	58.7 ± 11.3

DMH – 1,2 Dimethylhydrazine (40 mg/kg b.w.). Values are expressed as mean ± standard deviation, n = 5. No statistically significant differences were observed between the groups ($p < 0.05$).

Figure 2 summarizes the biochemical assessments performed to evaluate potential systemic toxicity of treatments. The parameters analyzed included indicators of nephrotoxicity (creatinine – **Fig. 2A**), hepatotoxicity (ALT – **Fig. 2B**), serum cholesterol (**Fig. 2C**), and blood glucose levels measured on days 0 and 28 (**Fig. 2D**). No statistically significant changes were detected in creatinine, cholesterol, or glucose levels between the treated and control groups, indicating the absence of renal or metabolic impairment. In contrast, a reduction in ALT levels was observed in rodents treated with doses of 125 or 250 mg/kg combined with the carcinogen DMH when compared to untreated rodents (negative control), which may suggest a mild hepatoprotective effect associated with these treatment conditions.

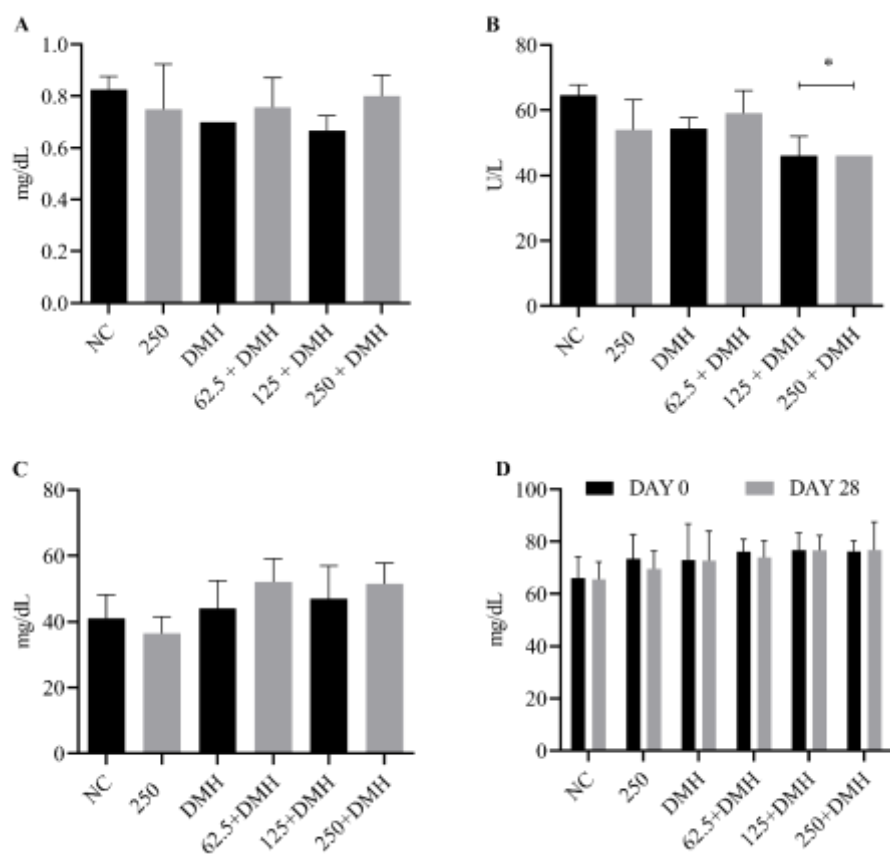


Figure 2. Serum levels of creatinine (A), alanine aminotransferase (ALT) (B), cholesterol (C) and blood glucose (D) obtained in Wistar rats treated with licuri oil (62.5, 125 and 250 mg/kg b.w.) plus DMH.

NC – Negative control; DMH – 1,2 Dimethylhydrazine (40 mg/kg b.w.). Values are expressed as mean $\pm$ standard deviation, n = 5. *Significantly different of NC group ($p < 0.05$).

4. Discussion

The present study demonstrates that LO is a safe natural compound with remarkable chemopreventive potential against chemically induced preneoplastic lesions in rat colon. The absence of clinical or biochemical signs of systemic toxicity following a single oral administration of 2000 mg/kg indicates a low acute toxicity profile, in accordance with GSH (OECD 423, 2002). These findings suggest that LO does not elicit systemic or organ-specific adverse effects, even at doses far exceeding those typically used for pharmacological or nutraceutical purposes.

Previous toxicological evaluations of *Syagrus coronata* fixed oil corroborate these findings, showing no mortality, genotoxicity, or clinical toxicity in rodent models at comparable doses (Souza et al., 2021; Barbosa et al., 2024). The biological safety of LO is likely related to its fatty acid composition and antioxidant bioactive constituents, with lauric acid predominating, alongside myristic, caprylic, oleic, and minor amounts of linoleic and other long-chain fatty acids (Bauer et al., 2013; Pereira et al., 2025). This balanced mixture of medium-chain saturated fatty acids (MCFAs) and unsaturated fatty acids enhances biocompatibility and favors rapid hepatic metabolism (Jadhav and Annapure, 2023).

MCFAs, such as lauric and caprylic acids, are efficiently absorbed and transported via the portal vein to the liver for β -oxidation, minimizing tissue accumulation and reducing the risk of organ stress or lipotoxicity (Papamandjaris et al., 1998). Concurrently, oleic and linoleic acids exert anti-inflammatory and membrane-stabilizing effects, contributing to cellular integrity and redox homeostasis (Carrillo et al., 2012; Poudyal et al., 2013; Santa-María et al., 2023). Together, these characteristics support the safe use of LO in pharmacological or nutraceutical contexts (Souza et al., 2021; Barbosa et al., 2024).

Given the use of LO in cooking or frying food, the impact of thermal processing on LO's stability and safety was also assessed. Subchronic administration of heated LO (HLO, 250 mg/kg for 28 days) did not produce systemic toxicity or behavioral changes, nor did it cause alterations in biochemical (creatinine, ALT, cholesterol, and glucose) or histopathological parameters. Furthermore,

heated oil did not exhibit a carcinogenic effect on the colon under the experimental conditions used. These data indicate that moderate heating of the LO does not compromise its safety.

The chemopreventive potential of LO was evaluated using the DMH-induced colon carcinogenesis model. DMH undergoes hepatic activation to generate methyl diazonium ions that induce DNA alkylation and oxidative stress in colon epithelial cells, triggering mutations, inflammation, and the formation of ACF, an early biomarker of preneoplastic transformation (Bird, 1987; Venkatachalam et al., 2020; Adrianto et al., 2024). LO treatment significantly reduced ACF formation, demonstrating a protective effect. Interestingly, the lowest dose elicited the most pronounced response, consistent with hormesis, where low doses of bioactive compounds trigger adaptive protective mechanisms while higher doses may result in metabolic saturation or compensatory effects (Mattson, 2008; Calabrese and Mattson, 2011; Calabrese, 2013).

The chemopreventive effect likely arises from the combined biological activities of LO's major fatty acids, including lauric, myristic, caprylic, oleic, and linoleic acids, which possess antioxidant, anti-inflammatory, and antiproliferative properties (Santa-María et al., 2023; Namachivayam et al., 2023; Wang et al., 2023; Manosalva et al., 2024). Previous studies support these effects: licuri fixed oil reversed rotenone-induced neurotoxicity (Amorim et al., 2024) and exhibited anti-inflammatory and antinociceptive properties without oral toxicity (Barbosa et al., 2024).

At the molecular level, lauric acid activates Nrf2/HO-1 signaling - main regulatory pathway of intracellular defense against oxidative stress (Yuan et al., 2024), upregulates antioxidant enzymes, and reduces lipid peroxidation and inflammatory mediators (Shaheryar et al., 2023; Onwuka and IGE, 2025). Myristic acid inhibits NF- κ B activation - a pivotal mediator of inflammatory responses (Liu et al., 2017), and cytokine release in microglial cells (Huang et al., 2023), while caprylic acid downregulates TLR4/NF- κ B signaling and decreases TNF- α levels in vitro and in vivo (Zhang et al., 2019; Zhang et al., 2022). Oleic acid enhances antioxidant enzymes and reduces pro-inflammatory

cytokines in experimental colitis model (Charlet et al., 2022), and linoleic acid improves endothelial function while attenuating inflammatory responses (Hung et al., 2023).

Additionally, LO's chemopreventive effects may also be mediated indirectly through modulation of the gut microbiota. Dietary lipids influence microbial composition and metabolism, thereby affecting intestinal inflammation and carcinogen metabolism (Mohammadi and Rudkowska, 2025). Given its reported antimicrobial activity (Bessa et al., 2016; Santos et al., 2019), LO may help establish a gut microbial balance that supports intestinal health and suppresses tumorigenic processes.

While this study provides strong evidence of LO's safety and chemopreventive potential, it is worth noting that future research should explore sex-specific responses, long-term progression to adenomas or carcinomas, and detailed molecular mechanisms, including oxidative stress modulation, anti-inflammatory pathways, apoptosis, and oil stability under varied conditions. Such studies will further elucidate LO's chemopreventive action and its translational potential in colorectal cancer prevention.

5. Conclusion

This study demonstrates that LO is safe and well-tolerated in Wistar Hannover rats, showing no signs of acute or subchronic toxicity. A single oral dose of 2000 mg/kg of LO and repeated administration of 250 mg/kg of HLO caused no clinical, biochemical, or histopathological alterations, confirming its low toxicological risk. In addition, LO significantly reduced DMH-induced preneoplastic lesions, indicating a pronounced chemopreventive effect against early colorectal carcinogenesis. Altogether, these results highlight LO as a safe natural compound with potential for use as a cooking oil and in dietary or nutraceutical interventions for the prevention of colorectal cancer.

Acknowledgment

The authors are grateful to Cooperativa Produtores e Agroextrativistas Frutos da Terra (Coopefrut), Miguel Calmon, Bahia, Brazil, for generously providing the licuri oil used in this study.

Funding sources

This work was supported by the São Paulo Research Foundation (FAPESP, Brazil; grant #2022/00806-4); National Council for Scientific and Technological Development (CNPq, Brazil) and Coordination for the Improvement of Higher Education Personnel (CAPES, Brazil).

Conflict of interest

The authors declare that there are no conflicts of interest.

References

2025 Dietary Guidelines Advisory Committee. Scientific report of the 2025 Dietary Guidelines Advisory Committee: advisory report to the Secretary of Health and Human Services and the Secretary of Agriculture. Washington (DC): U.S. Department of Health and Human Services; 2024. doi:10.52570/DGAC2025.

Acevedo-León D, Gómez-Abril SÁ, Sanz-García P, Estañ-Capell N, Bañuls C, Sáez G. The role of oxidative stress, tumor and inflammatory markers in colorectal cancer patients: A one-year follow-up study. *Redox Biol.* 2023;62:102662. doi:10.1016/j.redox.2023.102662

Adrianto AA, Riwanto I, Sadhana U, Setyawan H, Mahati E, Widyarini S, Wandita AAA, Paramita DK. Morphological changes and inflammation preceded the pathogenesis of 1,2-dimethylhydrazine-induced colorectal cancer. *Asian Pac J Cancer Prev.* 2024;25:2059-2067. doi:10.31557/APJCP.2024.25.6.2059

Amorim LC, Bezerra IC, da Silva AJ, Gubert P, Carvalho JM, Vieira LD, Alves JVO, Aguiar IFDS, Costa WK, de Melo Rego MJ, Pereira MC, Pitta MGdR, da Silva MV, dos Santos Correia MT, da Rosa MM. The antioxidant efficacy of *Syagrus coronata* fixed oil in reverting rotenone-induced neurotoxicity in mice. *Pharmacol Res - Nat Prod.* 2024;100045. doi:10.1016/j.prenap.2024.100045

Antoniassi R, Miranda PC, Ferreira GF, Vieira TMFS, Freitas SCD, Matsuura MISE. Nutritional evaluation of *Syagrus coronata* kernels and development of cookies prepared with cassava flour and licuri kernels. *Food Sci Technol*. 2021;42:e69720. doi.org/10.1590/fst.69720

Barbosa BVDDR, Alves JVO, Costa WK, Aguiar IFDS, Galvão LRL, Silva PMD, Silva LAD, Silva BVSD, Lima JS, Oliveira AM, Napoleão TH, Silva MVD, Correia MTDS. Almond fixed oil from *Syagrus coronata* (Mart.) Becc. has antinociceptive and anti-inflammatory potential, without showing oral toxicity in mice. *J Ethnopharmacol*. 2024;331:118283. doi: 10.1016/j.jep.2024.118283.

Bardelčíková A, Šoltys J, Mojžiš J. Oxidative Stress, Inflammation and Colorectal Cancer: An Overview. *Antioxidants (Basel)*. 2023;12:901. doi:10.3390/antiox12040901

Bauer LC, do Amaral Damasio JM, Da Silva MV, de Andrade Santana D, Gualberto SA, Simionato JI. Chemical characterization of pressed and refined licuri (*Syagrus coronata*) oils. *Acta Scientiarum. Technology*. 2013;35, 771-776. doi: 10.4025/actascitechnol.v35i4.20251

Belviso S, Ghirardello D, Giordano M, Ribeiro GS, Alves JS, Parodi S, Risso S, Zeppa G. Phenolic composition, antioxidant capacity and volatile compounds of licuri (*Syagrus coronata* (Martius) Beccari) fruits as affected by the traditional roasting process. *Food Res Int*. 2013;51:39-45. doi:10.1016/j.foodres.2012.11.012.

Bessa CMAS, do Nascimento RS, Alves RCC, Anselmo JM, da Silva APS, da Silva AG, Lima V LM, Tavares JF, da Silva LCN, da Silva MV, Correia MTS. *Syagrus coronata* seed oils have antimicrobial action against multidrug-resistant *Staphylococcus aureus*. *J Med Plants Res*. 2016; 10:310-317. doi: 10.5897/JMPR2016.6098

Bird RP. Observation and quantification of aberrant crypts in the murine colon treated with a colon carcinogen: preliminary findings. *Cancer Lett*. 1987;37:147-151. doi:10.1016/0304-3835(87)90157-1

Calabrese EJ, Mattson MP. Hormesis provides a generalized quantitative estimate of biological plasticity. *J Cell Commun Signal*. 2011;5:25-38. doi:10.1007/s12079-011-0119-1

Calabrese EJ. Biphasic dose responses in biology, toxicology and medicine: accounting for their generalizability and quantitative features. *Environ Pollut.* 2013;182:452-460. doi:10.1016/j.envpol.2013.07.046

Carrillo C, Cavia Mdel M, Alonso-Torre S. Role of oleic acid in immune system; mechanism of action; a review. *Nutr Hosp.* 2012;27:978-990. doi:10.3305/nh.2012.27.4.5783

Charlet R, Le Danvic C, Sendid B, Nagnan-Le Meillour P, Jawhara S. Oleic acid and palmitic acid from *Bacteroides thetaiotaomicron* and *Lactobacillus johnsonii* exhibit anti-inflammatory and antifungal properties. *Microorganisms.* 2022;10:1803. doi:10.3390/microorganisms10091803

George BP, Chandran R, Abrahamse H. Role of phytochemicals in cancer chemoprevention: insights. *Antioxidants (Basel).* 2021;10:1455. doi:10.3390/antiox10091455

Huang Q, Chen C, Zhang Z, Xue Q. Anti-inflammatory effects of myristic acid mediated by the NF- κ B pathway in lipopolysaccharide-induced BV-2 microglial cells. *Mol Omics.* 2023;19:726-734. doi:10.1039/d3mo00063j

Hung HC, Tsai SF, Chou HW, Tsai MJ, Hsu PL, Kuo YM. Dietary fatty acids differentially affect secretion of pro-inflammatory cytokines in human THP-1 monocytes. *Sci Rep.* 2023;13:5511. doi:10.1038/s41598-023-32710-5

Inocêncio ES, Buarque FS, Ferreira LFR, Soares CMF, Lima ÁS, Souza RLd. Exploring the potential of licuri (*Syagrus coronata*) using sustainable techniques and solvents for extracting bioactive compounds. *Sustainability.* 2025;17:1507. doi: 10.3390/su17041507

Jadhav HB, Annapure US. Triglycerides of medium-chain fatty acids: a concise review. *J Food Sci Technol.* 2023;60:2143-2152. doi:10.1007/s13197-022-05499-w

Katragadda HR, Fullana A, Sidhu S, Carbonell-Barrachina ÁA. Emissions of volatile aldehydes from heated cooking oils. *Food Chem.* 2010;120:59-65. doi: 10.1016/j.foodchem.2009.09.070.

Liu T, Zhang L, Joo D, Sun SC. NF- κ B signaling in inflammation. *Signal Transduct Target Ther*. 2017;2:17023. doi:10.1038/sigtrans.2017.23.

Manosalva C, Bahamonde C, Soto F, Leal V, Ojeda C, Cortés C, Alarcón P, Burgos RA. Linoleic acid induces metabolic reprogramming and inhibits oxidative and inflammatory effects in keratinocytes exposed to UVB radiation. *Int J Mol Sci*. 2024;25:10385. doi:10.3390/ijms251910385.

Mattson MP. Hormesis defined. *Ageing Res Rev*. 2008;7:1-7. doi:10.1016/j.arr.2007.08.007.

Menezes AV, de Souza DA, de Lima DP, et al. Fatty acids and volatile compound of cooked green licuri (*Syagrus coronata*) and naturally ripe licuri almonds from native flora, popularly consumed in Brazil. *Food Res Int*. 2024;191:114735. doi:10.1016/j.foodres.2024.114735

Mohammadi F, Rudkowska I. Dietary lipids, gut microbiota, and their metabolites: insights from recent studies. *Nutrients*. 2025;17:639. doi:10.3390/nu17040639

Namachivayam A, Valsala Gopalakrishnan A. Effect of lauric acid against ethanol-induced hepatotoxicity by modulating oxidative stress/apoptosis signalling and HNF4 α in Wistar albino rats. *Heliyon*. 2023;9:e21267. doi:10.1016/j.heliyon.2023.e21267

OECD (2002), *Test No. 423: Acute Oral toxicity - Acute Toxic Class Method*, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris, <https://doi.org/10.1787/9789264071001-en>.

Onwuka OM, Ige AO. Lauric acid treatment alleviates type-II-diabetes-induced osteoarthritis by activating joint Nrf2/HO-1 pathways resulting in enhanced synovial antioxidant activity and reduced inflammation. *Egypt J Basic Appl Sci*. 2025;12:220-236. doi:10.1080/2314808X.2025.2493007.

Papamandjaris AA, MacDougall DE, Jones PJ. Medium chain fatty acid metabolism and energy expenditure: obesity treatment implications. *Life Sci*. 1998;62:1203-1215. doi:10.1016/s0024-3205(97)01143-0

Pereira GSL, de Souza PT, Flozino GKM, et al. Evaluation of quality parameters, physicochemical and bioactive properties of licuri oil (*Syagrus coronata*). *Food Res Int*. 2025;208:116157. doi:10.1016/j.foodres.2025.116157

Poudyal H, Kumar SA, Iyer A, Waanders J, Ward LC, Brown L. Responses to oleic, linoleic and α -linolenic acids in high-carbohydrate, high-fat diet-induced metabolic syndrome in rats. *J Nutr Biochem*. 2013;24:1381-1392. doi:10.1016/j.jnutbio.2012.11.006

Roshandel G, Ghasemi-Kebria F, Malekzadeh R. Colorectal cancer: epidemiology, risk factors, and prevention. *Cancers (Basel)*. 2024;16:1530. doi:10.3390/cancers16081530

Santa-María C; López-Enríquez S; Montserrat-de la Paz S; Cruz-Gallego R; Ramos-Muñoz M; Martínez-Moya P; Madrid-Gallego R; Gutiérrez-Carranza ML; García-de-La-Torre C; Fornieles-Pérez CG; Medina-González A; Panadero I; Perona JS. Update on anti-inflammatory molecular mechanisms induced by oleic acid. *Nutrients*. 2023;15:224. doi:10.3390/nu15010224.

Senedese JM, Alves JM, Lima IM, de Andrade EA, Furtado RA, Bastos JK, Tavares DC. Chemopreventive effect of *Copaifera langsdorffii* leaves hydroalcoholic extract on 1,2-dimethylhydrazine-induced DNA damage and preneoplastic lesions in rat colon. *BMC Complement Altern Med*. 2013;13:3. doi: 10.1186/1472-6882-13-3.

Shankar G M, Swetha M, Keerthana CK, Rayginia TP, Anto RJ. Cancer chemoprevention: a strategic approach using phytochemicals. *Front Pharmacol*. 2022;12:809308. doi:10.3389/fphar.2021.809308

Shaheryar ZA, Khan MA, Hameed H, Zaidi SAA, Anjum I, Rahman MSU. Lauric acid provides neuroprotection against oxidative stress in mouse model of hyperglycaemic stroke. *Eur J Pharmacol*. 2023;956:175990. doi:10.1016/j.ejphar.2023.175990

Silva PFF, da Silva RR, Sarubbo LA, Guerra JMC. Production and optimization of biosurfactant properties using *Candida mogii* and licuri oil (*Syagrus coronata*). *Foods*. 2024;13(24):4029. doi:10.3390/foods13244029

Snetselaar LG, de Jesus JM, DeSilva DM, Stoody EE. Dietary Guidelines for Americans, 2020-2025: understanding the scientific process, guidelines, and key recommendations. *Nutr Today*. 2021;56(6):287-295. doi:10.1097/NT.0000000000000512

Souza Dos Santos B, Bezerra Filho CM, Alves do Nascimento Junior JA, Brust FR, Bezerra-Silva PC, Lino da Rocha SK, Krogfelt KA, Maria do Amaral Ferraz Navarro D, Tereza Dos Santos Correia M, Napoleão TH, Nascimento da Silva LC, Macedo AJ, Vanusa da Silva M, Guedes Paiva PM. Anti-staphylococcal activity of *Syagrus coronata* essential oil: Biofilm eradication and in vivo action on *Galleria mellonella* infection model. *Microb Pathog*. 2019;131:150-157. doi:10.1016/j.micpath.2019.04.009.

Souza TGS, da Silva MM, Feitoza GS, et al. Biological safety of *Syagrus coronata* (Mart.) Becc. fixed oil: cytotoxicity, acute oral toxicity, and genotoxicity studies. *J Ethnopharmacol*. 2021;272:113941. doi:10.1016/j.jep.2021.113941

Venkatachalam K, Vinayagam R, Arokia Vijaya Anand M, Isa NM, Ponnaiyan R. Biochemical and molecular aspects of 1,2-dimethylhydrazine (DMH)-induced colon carcinogenesis: a review. *Toxicol Res (Camb)*. 2020;9:2-18. doi:10.1093/toxres/tfaa004

Wang X, Zhang C, Bao N. Molecular mechanism of palmitic acid and its derivatives in tumor progression. *Front Oncol*. 2023;13:1224125. doi:10.3389/fonc.2023.1224125

Yuan L, Wang Y, Li N, Yang X, Sun X, Tian H, Zhang Y. Mechanism of action and therapeutic implications of Nrf2/HO-1 in inflammatory bowel disease. *Antioxidants*. 2024;13(8):1012. doi:10.3390/antiox13081012.

Zhang X, Xue C, Xu Q, et al. Caprylic acid suppresses inflammation via TLR4/NF- κ B signaling and improves atherosclerosis in ApoE-deficient mice. *Nutr Metab (Lond)*. 2019;16:40. doi:10.1186/s12986-019-0359-2

Zhang XS, Zhang P, Liu YH, Xu Q, Zhang Y, Li HZ, Liu L, Liu YM, Yang XY, Xue CY. Caprylic acid improves lipid metabolism, suppresses the inflammatory response and activates the

ABCA1/p-JAK2/p-STAT3 signaling pathway in C57BL/6J mice and RAW264.7 cells. *Biomed Environ Sci.* 2022;35:95-106. doi:10.3967/bes2022.014.