Comparative study of anti-inflammatory activity and acute toxicity of thick Myrtus communis L. leaf extracts cultivated in vivo and in vitro

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Inflammation is a fundamental protective biological mechanism; however, its chronic progression can lead to severe pathologies. Conventional anti-inflammatory drugs, such as corticosteroids and non-steroidal anti-inflammatory drugs, are often associated with considerable adverse effects. This necessitates the urgent search for novel, safer therapeutic agents, particularly among medicinal plants. *Myrtus communis* L. is well-recognized for its therapeutic properties, and its leaves have been traditionally utilized in folk medicine for the management of various inflammatory conditions.

The aim of the work was to comparatively evaluate the anti-inflammatory activity and acute toxicity of thick extracts obtained from the leaves of *Myrtus communis* L., cultivated in natural conditions (*in vivo*) and those obtained by microclonal propagation (*in vitro*), given the growing demand for effective and safe natural anti-inflammatory agents.

Materials and methods. Thick extracts of *Myrtus communis* leaves were obtained using fractional maceration with 70 % ethanol, followed by concentration via a rotary evaporator. Anti-inflammatory activity was assessed on the serotonin-induced edema model in white rats, by measuring the increase in paw volume. Experimental groups received the extracts (100 mg/kg) or ibuprofen (25 mg/kg). Additionally, the influence of the extracts on biochemical markers of inflammation (C-reactive protein, TBARS) and the blood protein profile was studied. Acute toxicity assessment was conducted in accordance with OECD guidelines, starting with a dose of 2000 mg/kg.

Results. The myrtle leaf extracts demonstrated potent anti-exudative activity, reducing paw edema by 33.55 % (*in vivo* extract) and 35.69 % (*in vitro* extract), results that are comparable to the effect observed with ibuprofen (42.11 %). The mechanism of action is likely linked to antagonism against serotonin receptors. Furthermore, the extracts significantly reduced the levels of inflammation and oxidative stress markers, concurrently contributing to the restoration of the serum protein profile. The extract obtained through microclonal propagation (*in vitro*) exhibited slightly superior efficacy, suggesting a potential advantage for this biotechnological approach. Acute toxicity assessment confirmed that both extracts belong to Category 5 of the toxicity classification (LD_{50} ≥5000 mg/kg for the *in vivo* thick extract and LD_{50} 2000–5000 mg/kg for the *in vitro* thick extract), confirming their low acute toxicity.

Conclusions. Concentrated *Myrtus communis* leaf extracts derived from plants grown under natural conditions and via microclonal propagation demonstrate marked anti-inflammatory and anti-exudative activity. Biotechnological cultivation approaches may offer a promising means of obtaining raw materials with enhanced biological efficacy.

Keywords: inflammation, common myrtle, serotonin-induced edema model, anti-exudative activity.

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Порівняльні дослідження протизапальної дії та гострої токсичності густих екстрактів листя Myrtus communis L., вирощеного в умовах in vivo та in vitro

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Запалення – ключовий захисний механізм, але його хронічна форма може призводити до тяжких патологій. Сучасні протизапальні препарати, як-от кортикоїди та нестероїдні протизапальні засоби, мають тяжкі побічні ефекти, тому актуальним є пошук нових, безпечніших засобів, зокрема серед лікарських рослин. *Myrtus communis* L. відомий завдяки терапевтичним властивостям, а його листя традиційно використовують для лікування запальних захворювань.

Мета роботи – здійснити порівняльне оцінювання протизапальної активності та гострої токсичності густих екстрактів листя *Myrtus communis* L., отриманих із рослин, що вирощені у природних умовах (*in vivo*) та за допомогою мікроклонального розмноження (*in vitro*), зважаючи на доцільність розробки ефективних і безпечних протизапальних засобів природного походження.

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Keywords: inflammation, common myrtle, serotonin-induced edema model, anti-exudative activity.

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Матеріали і методи. Густі екстракти листя *Myrtus communis* отримано шляхом дрібної мацерації 70 % етанолом та упарюванням у роторному випарювачі. Протизапальну активність оцінювали на моделі серотонінового набряку у білих щурів, визначали приріст об'єму лапи. Тварини з експериментальних груп отримували екстракти (100 мг/кг) або ібупрофен (25 мг/кг). Додатково вивчено вплив екстрактів на біохімічні маркери запалення (С-реактивний білок, ТБК-активні продукти) та білковий профіль крові. Гостру токсичність оцінювали згідно з рекомендаціями OECD, починаючи з дози 2000 мг/кг.

Результати. Встановлено виражену антиексудативну активність екстрактів листя мирту, що сприяли зменшенню набряку на 33,55 % (екстракт *in vivo*) та 35,69 % (екстракт *in vitro*); цей показник зіставний з дією ібупрофену (42,11 %). Механізм дії, ймовірно, пов'язаний з антагонізмом до серотонінових рецепторів. Екстракти також значно знижували рівні маркерів запалення й оксидативного стресу, відновлюючи білковий профіль крові. Екстракт, отриманий методом мікроклонального розмноження в умовах *in vitro*, мав дещо вищу ефективність, що свідчить про потенційну перевагу біотехнологічного підходу. Дослідження гострої токсичності дали змогу встановити, що обидва екстракти належать до 5 категорії токсичності (LD_{50} ≥5000 мг/кг для густого екстракту листя мирту, вирощеного в умовах *in vivo,* та LD_{50} 2000–5000 мг/кг для густого екстракту листя мирту, що вирощений в умовах *in vitro*). Ці дані підтверджують їхню низьку токсичність.

Висновки. Густі екстракти листя *Myrtus communis*, отримані з рослин, що вирощені у природних умовах і за допомогою мікроклонального розмноження, мають виражену протизапальну й антиексудативну активність. Біотехнологічні методи культивування можуть забезпечити отримання сировини з підвищеною біологічною активністю.

Ключові слова: запалення, мирт звичайний, модель серотонін-індукованого набряку, антиексудативна активність.

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Inflammation is an evolutionarily conserved process crucial for maintaining biological homeostasis. This dynamic defensive mechanism is triggered in response to various harmful inflamogens, including bacteria, viruses, fungi, protozoa, and helminth parasites [1]. During this process, immune and non-immune cells, such as monocytes, basophils, eosinophils, and neutrophils, are activated to eliminate pathogens and promote tissue repair and regeneration. The mechanism of inflammation involves a cascade of organized reactions encompassing both cellular and vascular events, alongside specific humoral secretions [2].

The inflammatory response comprises two main phases – acute and chronic – each mediated by unique mechanisms [2]. Acute inflammation, which exhibits a sudden onset and rapid resolution, is typically beneficial for the organism, serving as the first line of defense against infection and a potent activator of wound healing. Conversely, chronic inflammation is detrimental, characterized by a prolonged inflammatory response that leads to the loss of cellular balance and systemic biological damage [1]. Histologically, chronic inflammatory processes are distinguished by the infiltration of mononuclear cells, such as monocytes and lymphocytes, as well as the proliferation of fibroblasts, the formation of collagen fibers, and connective tissue, potentially culminating in granuloma formation [2].

Inflammation is regulated at the molecular level through the activation of numerous signaling pathways and the release of mediators. Primary inflammatory stimuli, including C-reactive protein (CRP), interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), mediate inflammation by activating corresponding receptors. These pro-inflammatory cytokines play a pivotal role in amplifying the inflammatory response, and if improperly controlled, can result in prolonged pain and impaired tissue healing [3].

Standard pharmaceutical agents used for inflammation management, such as corticoids and non-steroidal anti-inflammatory drugs, demonstrate high efficacy in controlling both acute and chronic inflammation. However, their prolonged use is frequently associated with the risk of serious complications, notably gastrointestinal bleeding [4]. These complications limit their long-term therapeutic application and stimulate the search for novel therapeutic molecules with improved efficacy and a safer profile.

In response to these challenges, medicinal plants and their derivatives are gaining increasing importance in modern medicine and pharmacology. Natural bioactive compounds often possess unique properties, allowing them to modulate specific biochemical targets and exert diverse therapeutic effects. This explains the accelerating interest in phytotherapy and the necessity of screening plant biological activity for the development of new pharmaceutical agents.

Myrtus communis L., or common myrtle, is one such focus of research, having been utilized in folk medicine for centuries due to its therapeutic attributes [5]. Analysis has revealed the presence of several key bioactive components across various parts of the plant: phenolic compounds (gallic and ellagic acids), flavonoids (quercetin-3-O-galactoside and quercetin-3-O-rhamnoside), hydrolysable tannins, anthocyanins, and volatile compounds (1,8-cineole, α-pinene, linalool, α-terpinyl acetate, and *trans*-caryophyllene) [6]. This multicomponent phytochemical profile enables a comprehensive therapeutic effect, which results not from the action of a single compound but from their synergy.

Unlike single-molecule drugs, the therapeutic action of myrtle extracts relies on the complementary influence of various compound classes, enabling them to impact multiple biochemical targets simultaneously. This accounts for the high efficacy of the extracts, even if the bioavailability of individual components, such as quercetin, may be inherently low [7].

A key mechanism of action for *Myrtus communis* L. involves its ability to modulate the activity of enzymes participating in inflammatory processes. Studies conducted on an acute colitis model demonstrated that the hydroalcoholic extract and the essential oil of myrtle effectively reduce the activity of myeloperoxidase (MPO). Since MPO is a marker of polymorphonuclear leukocyte migration and oxidative stress, its inhibition is a crucial aspect of anti-inflammatory therapy [8].

Myrtle extracts are also capable of modulating the expression of cytochrome P450 enzymes (CYPs), which are pivotal in the metabolism of xenobiotics and endogenous compounds. This capability aids in the prevention of chronic inflammation. Specifically, the extracts were noted to inhibit the expression of the CYP3A4 gene, which could potentially impact the metabolism of other therapeutic agents. This interaction elevates the discussion to a new level, indicating the necessity for further investigation into pharmacokinetic interactions. For instance, quercetin, one of myrtle's flavonoids, is a known inhibitor of CYP3A4 and CYP2C19 enzymes. Consequently, the application of myrtle extracts may affect the pharmacokinetics of other drugs metabolized by this enzymatic system [6].

Furthermore, it has been reported that myrtucommulone, a nonprenylated acylphloroglucinol found in *Myrtus communis* leaves, suppresses eicosanoid biosynthesis by inhibiting 5-lipoxygenase and cyclooxygenase-1 (*in vitro*). It also suppresses elastase release and the formation of reactive oxygen species (ROS) in activated polymorphonuclear leukocytes, thereby exhibiting potent anti-inflammatory effects [9].

Additionally, myrtle extracts may influence inflammasome activation, confirmed by their ability to inhibit the production of pro-inflammatory cytokines such as IL-1β. This multi-target action, directed at key steps of the inflammatory cascade, forms the basis of the plant's therapeutic potential [6].

Physiological changes were also evident in the gastric context, where pre-treatment with microencapsulated myrtle essential oil demonstrated a notable suppression of gastric lesions and acidity, correlating with a high percentage of healing and protection. Furthermore, it exerted a potent anti-inflammatory effect on the gastric mucosa by counteracting ethanol / HCl-induced gastric lipoperoxidation and preventing the depletion of antioxidant enzymes, specifically superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [10].

Moreover, myrtle extract effectively inhibited inflammation and fibrosis in the lung parenchyma using both prophylactic and therapeutic approaches. This effect may be attributed to a reduction in tissue inflammation and the suppression of oxidative stress [11].

Consequently, these studies collectively demonstrate that *Myrtus communis* L. leaf extracts possess significant anti-inflammatory effects, confirmed by improvements in various biochemical parameters and physiological changes observed in animal models. Nevertheless, further research is indispensable to fully elucidate the underlying mechanisms of action and definitively validate the traditional claims regarding the therapeutic utilization of this plant.

Aim

The aim of the work was to comparatively evaluate the anti-inflammatory activity and acute toxicity of thick extracts obtained from the leaves of *Myrtus communis* L., plants cultivated in natural conditions (*in vivo*) and those obtained by microclonal propagation (*in vitro*), given the growing demand for effective and safe natural anti-inflammatory agents.

Materials and methods

The object of the study was a thick extract of *Myrtus communis* L. leaves, sourced from plants cultivated under natural conditions (*in vivo*) and those obtained via microclonal propagation (*in vitro*). The raw plant material was shade-dried at room temperature for 5 days. The dried, ground material (particle size 3–5 mm) was then subjected to fractional maceration with 70 % ethanol (ratio 1:5) at room temperature for 3 days. The resulting extract was allowed to settle for 48 hours at a temperature not exceeding +10 °C, filtered, and concentrated to a thick consistency using a rotary evaporator at +50–55 °C.

The anti-inflammatory activity and acute toxicity of the thick *Myrtus communis* extracts were evaluated in the vivarium of the Educational and Medical Laboratory Center of Zaporizhzhia State Medical and Pharmaceutical University (Ukraine, Zaporizhzhia).

The study procedures adhered to the methodological recommendations for the preclinical study of non-steroidal anti-inflammatory drugs on the serotonin-induced edema model, induced by subplantar injection of 0.1 mL of 0.5 % serotonin solution. Experiments were conducted on non-linear white rats weighing 160−180 g, maintained under standard vivarium conditions. All animal experiments were performed in compliance with the rules of humane treatment of experimental animals as stipulated by the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986) and the Law of Ukraine "On Protection of Animals from Cruel Treatment" of 21.02.2006 No. 3447. The Bioethics Committee of Zaporizhzhia State Medical and Pharmaceutical University reviewed the materials presented in the article and found no ethical violations (meeting minutes No. 10, September 18, 2025).

To investigate the anti-inflammatory activity of the thick *Myrtus communis* leaf extracts, obtained under *in vivo* and *in vitro* conditions, and the reference drug ibuprofen (Geltec Private Limited, India, lot number AEU00223 04/2026), the experiment was conducted on animals divided into four groups (5 rats each). One hour prior to modeling acute aseptic inflammation (by subplantar injection of 0.1 mL of 0.5 % serotonin solution), the experimental groups received *Myrtus communis* extracts (100 mg/kg) or ibuprofen (25 mg/kg) administered intragastrically. The control group received only the vehicle. Paw volume was measured using an oncometer before and 60 minutes after the serotonin injection. Anti-inflammatory activity was assessed by the increase in paw volume, reflecting the degree of edema.

Anti-exudative activity (A, %) was calculated using the following formula:

$$A(\%) = \frac{(\Delta V\text{control} - \Delta V\text{experimental}) \times 100\ \%}{\Delta V\text{control}},$$

where ΔVexperimental – is the mean increase in paw volume in the experimental group or the comparison group; ΔVcontrol – is the mean increase in paw volume in the control group.

For the assessment of acute toxicity of the thick *Myrtus communis* extracts (both *in vivo* and *in vitro*), a protocol adapted from the OECD Guideline (Acute Oral Toxicity – Acute Toxic Class Method) was utilized [12,13]. The studies were performed on healthy non-pregnant female Wistar rats (8–12 weeks old, weighing 180–210 g), maintained under standard laboratory conditions with adherence to humane treatment protocols [14,15].

Prior to administration, the animals were fasted overnight, and subsequently fasted for an additional 3–4 hours after dosing [12]. Test samples, prepared as 20 % aqueous solutions of the extracts, were administered intragastrically (*per os*) via a gavage tube at a volume of 1 mL/100 g of body weight [16].

The study was conducted stepwise, utilizing 3 rats per stage:

1. In Step 1, a dose of 2000 mg/kg was administered to 3 rats for both the *Myrtus communis* (*in vivo*) and *Myrtus communis* (*in vitro*) extracts;

2. In Step 2, the same dose (2000 mg/kg) was administered to the next 3 female rats.

Following administration, the animals were kept under close observation: individual assessments were conducted at least once during the first 30 minutes, periodically throughout the first 24 hours (with particular attention during the initial 4 hours), and thereafter daily for a period of 14 days.

Statistical processing of the obtained data was performed using Microsoft Excel, applying the parametric Student's t-test. Differences were considered statistically significant at $p < 0.05$.

Results

The thick extract of *Myrtus communis* leaves presented as a viscous mass of dark brown color with an aromatic odor, soluble in purified water P and ethanol P. The yield of the thick extract amounted to 13.64 ± 1.55 %.

The results regarding the anti-exudative effect of the thick *Myrtus communis* leaf extracts, derived from plants grown under *in vivo* and *in vitro* conditions, and the reference drug ibuprofen on the development of serotonin-induced edema are presented in *Table 1*.

The subcutaneous administration of serotonin induced significant paw edema in animals of the control group. In rats treated with the thick *Myrtus communis* leaf extract (*in vivo*), a reduction in edema of 33.55 % was observed, while the administration of the thick *Myrtus communis* leaf extract (*in vitro*) resulted in an edema reduction of 35.69 %. The reference drug, ibuprofen, also exhibited anti-exudative activity, demonstrating 42.11 %.

Furthermore, in control group animals where edema was induced by the 0.5 % serotonin solution, a significant increase in CRP level was observed, rising to 4.82 ± 0.23 mg/L, which is more than four times the value found in the intact group (1.20 ± 0.10 mg/L); this confirms the activation of a systemic inflammatory reaction. The level of TBARS (thiobarbituric acid-reactive substances) also rose significantly – to 6.90 ± 0.35 nmol/mL versus 2.20 ± 0.14 nmol/mL in healthy animals This indicates the development of pronounced oxidative stress and intense lipid peroxidation, which constitutes one of the key mechanisms of tissue damage during exudation *(Table 2)*.

Concurrently, the control group exhibited a decrease in total protein to 60.20 ± 2.31 g/L (-17 %) and albumin to 30.60 ± 2.65 g/L (-20 %), which may be attributed to both impaired hepatic synthetic function and the exudation of proteins into the edematous tissues.

A statistically significant reduction in the levels of inflammation and oxidative stress markers was noted in the groups treated with the tested preparations compared to the control group. The thick *Myrtus communis* leaf extract (*in vitro*) demonstrated the most pronounced effect, showing a 53.11 % reduction in CRP and a 56.52 % reduction in TBARS, alongside a simultaneous increase in total protein and albumin by 15.95 % and 16.34 %, respectively. The thick *Myrtus communis* leaf extract (*in vivo*) reduced CRP levels by 51.45 % (2.34 ± 0.23 mg/L) and TBARS by 53.33 %, while promoting an increase in total protein by 13.62 % and albumin by 15.03 %. Ibuprofen, used as the reference drug, reduced CRP by 46.47 % and TBARS by 47.83 %, with an increase in protein indicators of 11.63 % for total protein and 11.76 % for albumin.

The acute toxicity test commenced with a dose of 2000 mg/kg and was conducted in two steps. Step 1: Upon administration of the 20 % thick extract solution of *Myrtus communis* cultivated *in vivo* at a dose of 2000 mg/kg, 0/3 animals perished; however, upon administration of the 20 % thick extract solution of *Myrtus communis* obtained via micrroclonal propagation (*in vitro*), 1/3 animals perished *(Table 3)*. Step 2: Upon administration of the 20 % extract solution, 0/3 animals in this group perished or were in a moribund state.

As all rats survived the administration of the thick *Myrtus communis* extracts (*in vivo* and *in vitro*) in the respective dosing groups, the study was concluded.

Discussion

The anti-inflammatory findings indicate that the thick *Myrtus communis* leaf extracts (*in vivo* and *in vitro*) demonstrate pronounced anti-exudative activity, comparable to the reference drug ibuprofen, achieving 33.55 % and 35.69 % efficacy, respectively, in the serotonin-induced paw edema model.

Consistent with methodological guidelines, this model is specific for elucidating compounds with an anti-serotonin mechanism. Given that inflammation in this model involves the release of serotonin, kinins, and other mediators, the high efficacy of the extracts suggests that their anti-inflammatory action is likely mediated by either serotonin receptor antagonism or the inhibition of serotonin release. This hypothesized mechanism complements previously established multi-target actions of myrtle phytocomponents, such as the inhibition of NF-κB and MAPK-dependent signaling cascades [17,18].

Beyond the anti-exudative effect, the study revealed a systemic anti-inflammatory and antioxidant action, as evidenced by alterations in biochemical markers. A significant reduction was observed in CRP, a key marker of systemic inflammation synthesized by the liver in response to infection or damage [19], decreasing by 51.45 % for the *in vivo* extract and 53.11 % for the *in vitro* extract compared to the control

Table 1. Influence on the development of serotonin-induced edema in rats (M ± m, n = 5)

Animal group	Dose, mg/kg	Increase in paw volume, mL	Anti-exudative activity, %
Control	–	8.56 ± 0.47	–
Thick *Myrtus communis* extract (*in vivo*)	100	5.69 ± 0.46*	33.55 %
Thick *Myrtus communis* extract (*in vitro*)	100	5.51 ± 0,67*	35.69 %
Ibuprofen	25	4.96 ± 1.53*	42.11 %

*: p < 0.05 compared to the control group.

Table 2. Changes in laboratory parameters in rats with serotonin-induced edema (M ± m, n = 5)

Group	C-reactive protein, mg/L	TBARS nmol/mL	Total protein, g/L	Albumin, g/L
Intact Animals	1.20 ± 0.10	2.20 ± 0.14	72.62 ± 2.07	38.40 ± 1.50
Control Group	4.82 ± 0.23	6.90 ± 0.35	60.20 ± 2.31	30.60 ± 2.65
Thick *M. communis* extract (*in vivo*)	2.34 ± 0.23*	3.22 ± 0.33*	68.40 ± 2.58*	35.20 ± 1.72*
	-51.45 %	-53.33 %	13.62 %	15.03 %
Thick *M. communis* extract (*in vitro*)	2.26 ± 0.21*	3.00± 0.28*	69.80 ± 2.32*	35.60 ± 3.44*
	-53.11 %	-56.52 %	15.95 %	16.34 %
Ibuprofen	2.58 ± 0.24*	3.60 ± 0.40*	67.20 ± 3.54*	34.20 ± 1.72*
	-46.47 %	-47.83 %	11.63 %	11.76 %

*: p < 0.05 compared to the control group.

Table 3. Mortality indicators in the studied groups

Drug name	Dosing group	Number of animals in group	Number of animal deaths
Thick *Myrtus communis* extract (*in vivo*) solution	Step 1 Dosing Group	3	0
	Control Dosing Group	3	0
Thick *Myrtus communis* extract (*in vitro*) solution	Step 1 Dosing Group	3	1
	Control Dosing Group	3	0

group. This outcome suggests that myrtle extracts possess a broad spectrum of activity affecting systemic inflammatory processes. Furthermore, a substantial reduction was recorded in TBARS, markers of lipid peroxidation, by 53.33 % and 56.52 %, respectively. This confirms the potent antioxidant properties of the extracts, which are capable of counteracting oxidative stress, a phenomenon playing a central role in maintaining inflammatory processes [20]. The restoration of the blood protein profile, specifically the increased levels of total protein and albumin, is a direct physiological consequence of reduced exudation and indicates the vascular-protective potential of the extracts [19].

A comparison of the efficacy of the extracts obtained under different cultivation methods points to the potential advantage of biotechnological techniques. The marginally superior activity of the *in vitro* extract in reducing edema and lowering inflammatory markers suggests the possibility of optimizing cultivation conditions (e. g., nutrient media composition, light intensity, temperature) to stimulate the enhanced production of secondary metabolites [21]. Consequently, microclonal propagation emerges as a promising technology for obtaining standardized raw materials with improved therapeutic characteristics.

A critically important aspect of the study was the acute toxicity assessment, which confirmed the high safety profile of both extracts. According to international classification, both extracts fall into Toxicity Category 5 (LD_{50} ≥5000 mg/kg for *in vivo* and LD_{50} 2000–5000 mg/kg for *in vitro*), indicating their classification as non-toxic [8]. This finding aligns with the research of other scientists and is significant [22,23]. As it allows myrtle to be positioned as a safe alternative to conventional anti-inflammatory drugs, which are frequently associated with severe adverse effects, particularly gastrointestinal bleeding.

Conclusions

1. The thick extracts derived from *Myrtus communis* leaves, obtained from both conventional cultivation (*in vivo*) and microclonal propagation (*in vitro*), demonstrated distinct anti-inflammatory and anti-exudative efficacy. The extracts effectively reduced edema in the rat model of serotonin-induced inflammation, exhibiting activity comparable to that of the reference drug, ibuprofen.

2. The tested extracts significantly lowered the levels of inflammation and oxidative stress markers, specifically CRP and TBARS (thiobarbituric acid-reactive substances), while simultaneously contributing to the restoration of the blood protein profile. This evidence confirms their systemic anti-inflammatory and vascular-protective potential.

3. The thick extract obtained through *in vitro* microclonal propagation displayed marginally superior anti-exudative activity (35.69 %) and was more effective in reducing inflammatory markers compared to the naturally grown *in vivo* extract (33.55 %). This observation suggests a potential advantage in utilizing biotechnological cultivation methods for obtaining raw material with enhanced biological activity.

4. Both *Myrtus communis* extracts are classified as having low acute toxicity, belonging to Category 5 of the international classification (LD_{50} ≥5000 mg/kg for the *in vivo* extract and LD_{50} 2000–5000 mg/kg for the *in vitro* extract), which underscores their favorable safety profile.

Prospects for further research. Future research efforts should focus on the precise identification of the active components within *Myrtus communis* extracts, a detailed investigation of their molecular mechanisms of action, the development of novel pharmaceutical formulations, and expanded toxicological studies to definitively confirm their therapeutic potential as a safe anti-inflammatory agent.

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