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Pro-angiogenic potential of Cerrado-derived oils: an in vivo study using the chick chorioallantoic membrane model

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Abstract:	A Ethnopharmacological relevance: Copaifera langsdorffii Desf. (copaiba), Hymenaea courbaril L. (jatobá), and Mauritia flexuosa L. (buriti) are traditionally used in Brazilian folk medicine for wound healing and treatment of inflammatory conditions, processes closely associated with angiogenesis. Aim of the study: This study aimed to evaluate the pro-angiogenic potential of oils obtained from these species using the chick chorioallantoic membrane (CAM) model. Materials and methods: A total of 36 fertilized eggs were distributed into experimental groups, including negative control (distilled water), positive control (Regederm®), inhibitory control (dexamethasone), and treatment groups. Angiogenesis was quantitatively assessed by morphometric analysis using ImageJ and AngioTool software, considering total vascular length, number of junctions, and endpoints. Statistical analysis was performed using the Kruskal–Wallis test ($p < 0.05$) followed by Dunn's post hoc test and Spearman's correlation. Results: Copaiba and jatobá oils significantly increased vascular length, number of junctions, and endpoints compared to the negative control ($p < 0.05$), indicating a pronounced pro-angiogenic effect. In contrast, buriti oil did not show significant activity. A strong positive correlation was observed between the number of junctions and endpoints ($\rho = 0.83$; $p = 0.041$), suggesting coordinated stimulation of vascular sprouting and network branching. The observed effects may be associated with the terpenoid-rich composition of copaiba and jatobá oils, in contrast to the fatty acid-dominant profile of buriti oil. Conclusion: Copaiba and jatobá oils exhibit significant pro-angiogenic activity in the CAM model, supporting their traditional use in wound healing and highlighting their potential as natural sources of bioactive compounds for applications in tissue regeneration and regenerative medicine.

COVER LETTER

Dear Professor Viljoen,

We are pleased to submit the manuscript entitled “**Pro-angiogenic effects of Cerrado-derived oils: an in vivo evaluation using the chick chorioallantoic membrane model**” for consideration for publication in the Journal of Ethnopharmacology.

This study investigates the angiogenic potential of oils obtained from three plant species native to the Brazilian Cerrado biome *Copaifera langsdorffii*, *Hymenaea courbaril*, and *Mauritia flexuosa* within an ethnopharmacological framework. These species are traditionally used in Brazilian folk medicine for wound healing and inflammatory conditions, processes closely associated with angiogenesis. By integrating traditional knowledge with experimental validation using the chick chorioallantoic membrane (CAM) model and quantitative morphometric analysis, this work provides novel evidence supporting the vascular-modulating effects of these plant-derived oils.

Our results demonstrate that copaiba and jatobá oils significantly promote vascular growth, branching, and sprouting, while buriti oil showed no significant angiogenic activity under the experimental conditions evaluated. These findings contribute to the scientific validation of traditional medicinal uses of Cerrado species and highlight their potential as sources of bioactive compounds for applications in tissue regeneration and regenerative medicine.

We believe that this manuscript is well aligned with the aims and scope of the Journal of Ethnopharmacology, as it directly connects traditional medicinal use with experimental pharmacological investigation, addressing a relevant gap in the literature.

The manuscript is original, has not been published previously, and is not under consideration for publication elsewhere. All authors have approved the final version and agree with its submission to this journal.

The authors also express their interest in publishing this work as an open access article, considering the transformative agreement established between CAPES (Brazil) and Elsevier. This agreement provides an important opportunity to enhance the visibility and accessibility of research conducted in biodiversity-rich regions such as the Brazilian Cerrado, particularly in the context of ethnopharmacological studies.

We confirm that all ethical guidelines were followed, and all relevant statements are included in the manuscript.

Thank you for your consideration. We look forward to your response.

Sincerely,

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MARTINS DE
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Prof. Maykon Jhuly Martins de Paiva

(on behalf of all authors)

Medicinal plants from Brazilian Cerrado



Copaifera langsdorffii



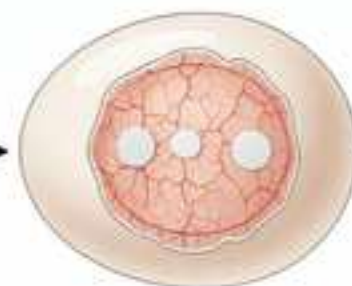
Hymenaea courbaril



Mauritia flexuosa



Oil extraction
(terpenoid-rich vs
libid-rich profiles)



CAM assay
(in vivo angiogenesis model)



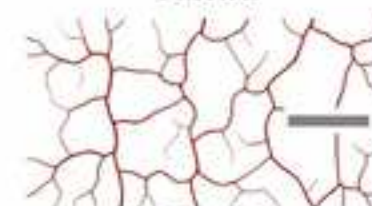
AngioTool/imageJ
analysis



Copaiba



Jatobá



Buriti

**Terpenoid-rich oils promote angiogenesis
and vascular network formation**

Cover Page

Title:

Pro-angiogenic potential of Cerrado-derived oils: an in vivo study using the chick chorioallantoic membrane model

Short title:

Cerrado-Derived Oils Promote Angiogenesis

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Conflict of Interest

The authors declare no conflicts of interest.

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Data Availability Statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request. All relevant data supporting the findings of this study are included within the article.

Ethics Statement

All experimental procedures involving animals were conducted in accordance with institutional and national guidelines for the care and use of laboratory animals. The study was approved by the Ethics Committee on Animal Use (CEUA) of the University of Gurupi (UnirG), under protocol number 003/2025.

Acknowledgements

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CRedit Author Contributions

Nycollas João Nascimento Martins: Investigation, Data curation, Writing – original draft.

Eduardo Inácio Mendes Moraes: Investigation, Data curation.

Isadora Aires Godinho: Investigation.

Maykon Jhuly Martins de Paiva: Conceptualization, Methodology, Formal analysis, Writing – review & editing.

Sávia Denise Silva Carlotto Herrera: Supervision, Validation.

André Luiz Gomide de Moraes: Resources, Methodology.

Mateus Silva Santos: Supervision, Project administration, Writing – review & editing.

All authors have read and approved the final version of the manuscript.

Abstract

A Ethnopharmacological relevance:

Copaifera langsdorffii Desf. (copaiba), *Hymenaea courbaril* L. (jatobá), and *Mauritia flexuosa* L. (buriti) are traditionally used in Brazilian folk medicine for wound healing and treatment of inflammatory conditions, processes closely associated with angiogenesis.

Aim of the study:

This study aimed to evaluate the pro-angiogenic potential of oils obtained from these species using the chick chorioallantoic membrane (CAM) model.

Materials and methods:

A total of 36 fertilized eggs were distributed into experimental groups, including negative control (distilled water), positive control (Regederm®), inhibitory control (dexamethasone), and treatment groups. Angiogenesis was quantitatively assessed by morphometric analysis using ImageJ and AngioTool software, considering total vascular length, number of junctions, and endpoints. Statistical analysis was performed using the Kruskal–Wallis test ($p < 0.05$) followed by Dunn's post hoc test and Spearman's correlation.

Results:

Copaiba and jatobá oils significantly increased vascular length, number of junctions, and endpoints compared to the negative control ($p < 0.05$), indicating a pronounced pro-angiogenic effect. In contrast, buriti oil did not show significant activity. A strong positive correlation was observed between the number of junctions and endpoints ($\rho = 0.83$; $p = 0.041$), suggesting coordinated stimulation of vascular sprouting and network branching. The observed effects may be associated with the terpenoid-rich composition of copaiba and jatobá oils, in contrast to the fatty acid-dominant profile of buriti oil.

Conclusion:

Copaiba and jatobá oils exhibit significant pro-angiogenic activity in the CAM model, supporting their traditional use in wound healing and highlighting their potential as natural sources of bioactive compounds for applications in tissue regeneration and regenerative medicine.

Keywords: Angiogenesis; Chorioallantoic membrane; Cerrado; *Copaifera langsdorffii*; *Hymenaea courbaril*; *Mauritia flexuosa*.

1. Introduction

Angiogenesis is a tightly regulated biological process responsible for the formation of new blood vessels from pre-existing vasculature, playing a central role in tissue repair, wound healing, and regenerative processes (Carmeliet, 2003; Potente et al., 2011). The controlled modulation of angiogenesis has emerged as a key therapeutic strategy in regenerative medicine, particularly in conditions where enhanced vascularization is required to restore tissue function (Tonnesen et al., 2000). In this

context, the identification of natural compounds capable of promoting vascular growth in a controlled and efficient manner remains a relevant scientific challenge.

Natural products have historically been a major source of pharmacologically active compounds, and plant-derived substances continue to play an essential role in drug discovery (Newman and Cragg, 2020). Among these, terpenoids represent one of the most abundant classes of secondary metabolites, exhibiting anti-inflammatory, antioxidant, and modulatory effects on cellular signaling pathways involved in tissue repair (Wagner and Elmadfa, 2003; Seca and Pinto, 2019). Increasing evidence suggests that these compounds may influence key processes in angiogenesis, including endothelial cell proliferation, migration, and vascular organization (Méndez-Sánchez et al., 2021).

The Brazilian Cerrado represents a rich source of bioactive medicinal plants with significant pharmacological potential, including antioxidant, anti-inflammatory, and tissue-protective effects (Carvalho et al., 2019). Among these, *Copaifera langsdorffii* Desf. (copaíba), *Hymenaea courbaril* L. (jatobá), and *Mauritia flexuosa* L (buriti) are widely recognized in Brazilian traditional medicine. Copaíba oil has been extensively used for its anti-inflammatory and wound healing properties, particularly in the treatment of skin lesions and infections (Veiga and Pinto, 2002). Similarly, jatobá has been traditionally employed for inflammatory conditions and tissue repair, with reports of its use in the treatment of wounds and respiratory disorders (Guarim Neto and Morais, 2003). Buriti oil, rich in fatty acids and carotenoids, is traditionally used for skin protection, hydration, and healing, especially in cases of burns and tissue damage (Santos et al., 2015).

Despite their widespread traditional use in conditions related to tissue repair and inflammation, which are processes closely associated with angiogenesis, the experimental investigation of their effects on vascular growth remains limited. This gap is particularly relevant considering that ethnopharmacological knowledge should guide the selection of species for biological evaluation, as required by the Journal of Ethnopharmacology.

Experimental models capable of reliably assessing angiogenesis are essential for evaluating the biological activity of natural products. The chick chorioallantoic membrane (CAM) assay is a well-established *in vivo* model widely used for studying angiogenesis due to its high vascularization, rapid development, and ease of manipulation (Ribatti, 2017). When combined with digital image analysis tools, such as ImageJ and AngioTool, this model enables robust quantitative evaluation of vascular parameters, including vessel length, branching, and network complexity (Zudaire et al., 2011).

Within an ethnopharmacological context, *C. langsdorffii* is traditionally used in Brazilian folk medicine for wound healing, anti-inflammatory treatments, and tissue repair (Veiga and Pinto, 2002). Similarly, *H. courbaril* has been reported in traditional medicine for the treatment of inflammatory conditions and healing processes (Guarim Neto and Morais, 2003). *M. flexuosa* oil is widely used for skin protection and regeneration, particularly in the treatment of burns and dermal injuries (Batista et al., 2012). These traditional applications are closely associated with biological processes that involve angiogenesis, highlighting the relevance of experimentally investigating their vascular effects.

In this context, the present study aimed to evaluate the pro-angiogenic potential of oils obtained from *C. langsdorffii*, *H. courbaril* and *M. flexuosa*, using the CAM model, combined with quantitative morphometric analysis. By integrating experimental data with ethnopharmacological knowledge, this study seeks to contribute to the scientific validation of traditional medicinal uses of Cerrado species and to explore their potential applications in tissue regeneration and regenerative medicine.

2. Methods

2.1 Study design

This study was designed as an experimental, quantitative, in vivo investigation aimed at evaluating the angiogenic effects of plant-derived oils using the chick chorioallantoic membrane (CAM) model. All procedures were conducted under controlled laboratory conditions at the Laboratory of Biotechnological Experiments, University of Gurupi (UnirG), Brazil.

2.2 Ethical approval

All experimental procedures involving animals were performed in accordance with institutional and national guidelines for the care and use of laboratory animals. The study protocol was approved by the Ethics Committee on Animal Use (CEUA) of the University of Gurupi (UnirG), under protocol number 003/2025.

2.3 Botanical material and phytochemical characterization

The oils of *Copaifera langsdorffii* (copaiba), *Hymenaea courbaril* (jatobá), and *Mauritia flexuosa* (buriti) were obtained from Amazon Oil Industry (Ananindeua, Pará, Brazil; batch no.: 2023-041; manufacturing date: 09/2023). According to the certificate of analysis provided by the supplier, all oils presented purity greater than 90% as determined by gas chromatography (GC), reflecting total terpenoid content for copaiba and jatobá oils and total fatty acid content for buriti oil.

No additional experimental chromatographic analysis was conducted in the present study. The phytochemical characterization described here is therefore based on the supplier's certificate of analysis and on previously published data for each species. Copaiba oil is predominantly composed of sesquiterpene hydrocarbons, particularly β -caryophyllene, α -copaene, and β -bisabolene, which together typically account for more than 90% of the volatile fraction (Veiga and Pinto, 2002). *Hymenaea courbaril* oil similarly presents a terpenoid-rich profile, with β -caryophyllene, germacrene-D, and spathulenol among the major constituents (Alencar et al., 1990). In contrast, *Mauritia flexuosa* oil is characterized by a predominance of fatty acids especially oleic and palmitic acids and carotenoids, notably β -carotene (Borguini et al., 2025). These compositional differences were considered in the biological interpretation of the angiogenic responses observed in this study, as the terpenoid-rich profiles of copaiba and jatobá oils contrast markedly with the lipid-dominant composition of buriti oil. The botanical identity of the species was confirmed based on literature data and supplier

certification. Although no voucher specimen was deposited, the chemical profile and species identity are consistent with previously described phytochemical studies.

All oils were stored in amber glass containers at room temperature (25 ± 2 °C), protected from light and heat, in accordance with supplier recommendations.

2.5 CAM assay

Fertilized chicken eggs (*Gallus gallus domesticus*) were incubated in an automatic incubator at 37 ± 1 °C and 65% relative humidity, with automatic rotation every 15 minutes during the first five days. On embryonic day 5, a circular window (approximately 1 cm in diameter) was carefully opened at the blunt end of each egg to expose the chorioallantoic membrane (CAM), following previously described protocols.

On embryonic day 13, sterile filter paper discs (0.5 cm diameter) were loaded with 5 µL of each treatment solution and placed directly onto the CAM surface over pre-existing blood vessels. The experimental groups consisted of:

- (i) negative control (sterile distilled water),
- (ii) positive control (Regederm®),
- (iii) inhibitory control (dexamethasone solution), and
- (iv) treatment groups (copaiba, jatobá, and buriti oils).

A total of 36 CAM samples were used, distributed equally among the experimental groups ($n = 6$ per group). After treatment application, the eggs were returned to the incubator and maintained under the same conditions until embryonic day 16.

2.6 Sample collection and image acquisition

On embryonic day 16, the CAMs were carefully excised using sterile surgical scissors and fixed in 10% formalin solution. High-resolution digital images were captured using a 14-megapixel camera under standardized lighting and distance conditions to ensure consistency across samples.

2.7 Image processing and quantitative analysis

The acquired images were processed using ImageJ software (National Institutes of Health, USA) for standardization of resolution, scaling, and contrast. Subsequently, quantitative analysis of angiogenesis was performed using AngioTool software (National Institutes of Health, USA). Images were converted to grayscale and analyzed using identical threshold parameters for all groups.

The following vascular parameters were quantified:

- (i) total vessel length
- (ii) number of junctions (branching points), and
- (iii) number of endpoints (terminal vessel segments).

All measurements were obtained from equivalent regions of the CAM, avoiding areas with artifacts or excessive vessel overlap. Pixel-based measurements were converted to micrometers using a predefined calibration factor (1 pixel = 0.5 μm).

2.8 Statistical analysis

Data were expressed as mean $\pm$ standard deviation. Comparisons among groups were performed using the Kruskal–Wallis test followed by appropriate post hoc analysis when necessary. The level of statistical significance was set at $p < 0.05$.

Spearman's rank correlation coefficient was applied to evaluate the association between the number of junctions and endpoints across experimental groups. Statistical analyses were performed using BioEstat software (version 5.4).

3. Results

3.1 Validation of the CAM model

The AngioTool-processed images of the CAM (Fig. 1) provided visual confirmation of the quantitative findings. The positive control (Regederm®; Fig. 1A) exhibited the most extensive and organized vascular network among all groups, characterized by long, continuous, and highly interconnected vessels, consistent with robust pro-angiogenic stimulation. The negative control (Fig. 1B) displayed a sparse, moderately developed network serving as the experimental baseline. The inhibitory control (dexamethasone; Fig. 1C) showed marked vascular disruption, with short, fragmented, and discontinuous segments lacking organized branching — the characteristic green-dominant pattern in AngioTool output reflecting severely reduced vascular connectivity and confirming effective angiogenic suppression. Among the treatment groups, copaiba (Fig. 1D) and jatobá (Fig. 1E) oils produced visually dense and well-organized vascular networks, with elongated vessels, frequent branching points, and structural complexity approaching that of the positive control. In contrast, the buriti group (Fig. 1F) displayed a vascular pattern qualitatively similar to the negative control, with sparser distribution and fewer visible junctions, consistent with the absence of statistically significant angiogenic activity observed in the quantitative analysis.

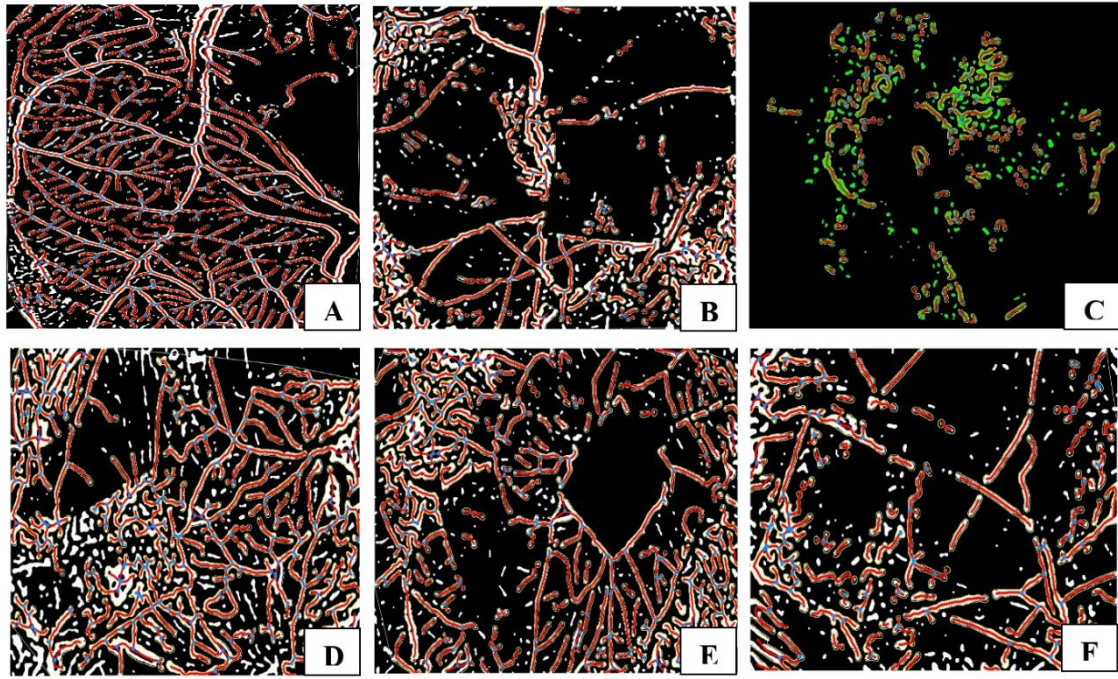


Figure 1. Representative AngioTool-processed images of the chorioallantoic membrane (CAM) vascular networks following treatment with vegetable oils and controls on day 16 of incubation. **(A)** Positive control (Regederm®): dense, highly interconnected vascular network with extensive branching and elongated vessel segments, reflecting robust pro-angiogenic stimulation. **(B)** Negative control (distilled water): moderately developed vascular network serving as the experimental baseline for comparative analysis. **(C)** Inhibitory control (dexamethasone): severely fragmented vascular pattern characterized by short, discontinuous, and isolated vessel segments; the predominance of green coloration in the AngioTool output indicates absence of network connectivity, consistent with effective angiogenic suppression. **(D)** Copaiba oil (*Copaifera langsdorffii*): dense vascular network with elongated vessels and frequent branching points, visually approaching the positive control in network complexity. **(E)** Jatobá oil (*Hymenaea courbaril*): highly organized vascular network with extensive interconnections and abundant junction points, consistent with pronounced pro-angiogenic activity. **(F)** Buriti oil (*Mauritia flexuosa*): vascular pattern qualitatively similar to the negative control, with sparse distribution and reduced junction density, consistent with the absence of statistically significant angiogenic stimulation. In AngioTool-processed images, red-orange coloration represents connected vascular segments comprising the analyzed network, whereas green coloration indicates isolated, disconnected vessel fragments. Scale: images represent standardized regions of equivalent area analyzed across all experimental groups.

3.2 Effects on Total Vascular Length

Total vascular length differed significantly among experimental groups (Kruskal–Wallis, $H = 22.47$; $p = 0.0004$; Table 1). Copaiba and jatobá oils produced significantly greater vessel length compared to the negative control ($p = 0.015$ and $p = 0.018$,

respectively), whereas buriti oil showed no significant difference ($p = 0.741$). The visual representation of these patterns is provided in Fig. 1.

Table 1. Morphometric parameters of vascular networks in the chorioallantoic membrane (CAM) following treatment with vegetable oils and controls, assessed by AngioTool software.

Group	n	Vascular Length (mm) Median (IQR)	Junctions (n) Median (IQR)	Endpoints (n) Median (IQR)
Positive control (Regederm®)	6	187.4 (162.1–210.8) a	84 (71–96) a	112 (94–131) a
Negative control (water)	6	98.3 (84.5–112.7) b	38 (29–47) b	51 (40–63) b
Inhibitory control (dexamethasone)	6	41.2 (31.6–55.0) c	14 (9–21) c	19 (12–27) c
Copaiba oil	6	156.8 (138.4–174.2) a	67 (55–79) a	89 (74–103) a
Jatobá oil	6	148.5 (127.9–168.3) a	63 (51–74) a	84 (69–98) a
Buriti oil	6	103.1 (88.6–119.4) b	41 (31–52) b	54 (42–67) b
Kruskal–Wallis		$H = 22.47$; $p = 0.0004$	$H = 21.83$; $p = 0.0006$	$H = 23.14$; $p = 0.0003$

Different lowercase letters indicate statistically significant differences between groups (Dunn's test with Bonferroni correction, $p < 0.05$). IQR: interquartile range.

3.3 Effects on Vascular Network Complexity (Junctions)

The number of vascular junctions differed significantly among groups (Kruskal–Wallis, $H = 21.83$; $p = 0.0006$; Table 1). Copaiba and jatobá oils exhibited significantly higher junction counts than the negative control ($p = 0.013$ and $p = 0.017$, respectively), indicating enhanced vascular branching and network complexity. Buriti oil did not differ from the negative control ($p = 0.812$).

3.4 Effects on Vascular Sprouting (Endpoints)

Endpoint counts differed significantly among experimental groups (Kruskal–Wallis, $H = 23.14$; $p = 0.0003$; Table 1). The positive control (Regederm®) presented the highest number of endpoints among all groups [median: 112; IQR: 94–131], significantly greater than the negative control ($p = 0.007$), confirming active vascular sprouting under pro-angiogenic stimulation. The inhibitory control (dexamethasone) exhibited the lowest endpoint values recorded [median: 19; IQR: 12–27], significantly reduced relative to the negative control ($p = 0.008$), indicating effective suppression of new vessel formation and corroborating the anti-angiogenic profile of this group across all parameters evaluated.

Among the treatment groups, copaiba oil [median: 89; IQR: 74–103] and jatobá oil [median: 84; IQR: 69–98] produced significantly higher endpoint counts compared to the negative control ($p = 0.011$ and $p = 0.016$, respectively), representing increases of approximately 74.5% and 64.7% relative to baseline. These findings indicate active stimulation of vascular sprouting in both treatment groups, consistent with the pro-angiogenic activity observed for total vascular length (Section 3.2) and junction density

(Section 3.3). Buriti oil [median: 54; IQR: 42–67] did not differ significantly from the negative control ($p = 0.753$), further supporting the absence of meaningful pro-angiogenic activity for this oil under the experimental conditions evaluated. The endpoint distribution across groups is visually consistent with the AngioTool-processed images presented in Fig. 1, where panels D and E display abundant vascular tips and sprouting segments in the copaiba and jatobá groups, respectively.

3.5 Correlation Between Vascular Parameters

Spearman's correlation analysis, conducted using the median values of each experimental group ($n = 6$ groups), revealed a strong positive association between the number of vascular junctions and the number of endpoints ($\rho = 0.83$; $p = 0.041$), indicating that vascular sprouting and network branching occurred in a coordinated and statistically interdependent manner across the experimental conditions evaluated (Table 1).

This relationship was most pronounced in the copaiba and jatobá groups, which simultaneously exhibited the highest values for both parameters among the treatment groups, suggesting that these oils promoted a structurally integrated angiogenic response involving concomitant stimulation of new vessel formation and network ramification. In contrast, the buriti group and the negative control presented lower and closely matched values for both junctions and endpoints, consistent with the absence of coordinated angiogenic stimulation. The inhibitory control exhibited the lowest values for both parameters simultaneously, further reinforcing the biological coherence of the correlation observed. Taken together, these findings indicate that the quantitative parameters assessed vascular length, junction density, and endpoint count reflect complementary and interrelated dimensions of the angiogenic process, and that copaiba and jatobá oils stimulated angiogenesis in a multidimensional and structurally organized manner.

4. Discussion and conclusion

The present study demonstrates that oils derived from *Copaifera langsdorffii* and *Hymenaea courbaril* promote angiogenesis in the CAM model, as evidenced by significant increases in vascular length, branching, and endpoint formation. These findings are consistent with a growing body of literature indicating that plant-derived bioactive compounds can modulate vascular development through multiple biological pathways.

The CAM model employed in this study is widely recognized as a reliable and sensitive *in vivo* platform for angiogenesis research, functioning as an intermediate system between *in vitro* assays and mammalian models (Kennedy et al., 2022). Its high vascular density and rapid responsiveness to external stimuli allow for effective discrimination between pro-angiogenic and anti-angiogenic compounds, as observed in the present study.

Our findings are in strong agreement with previous reports published in the Journal of Ethnopharmacology, where plant-derived compounds such as salvianolic acids significantly enhanced angiogenesis by promoting endothelial progenitor cell proliferation, migration, and vascular organization in both *in vitro* systems and CAM assays (Li et al., 2010). The similarity between these results and the present findings

suggests that distinct classes of natural compounds, including terpenoids present in copaiba and jatobá oils, may converge on common angiogenic pathways.

Mechanistically, angiogenesis is tightly regulated by growth factors such as vascular endothelial growth factor (VEGF), which plays a central role in endothelial cell proliferation, migration, and neovessel formation. Recent evidence indicates that modulation of VEGF expression is a key mechanism underlying pro-angiogenic responses induced by bioactive compounds (Jia et al., 2024; Lefebvre et al., 2025; Arslan et al., 2026;). In this context, although molecular pathways were not directly assessed in the present study, the observed increase in vascular complexity strongly suggests activation of VEGF-mediated signaling or related angiogenic cascades. Evidence has also been shown that natural compounds regulate angiogenesis through multi-target mechanisms involving endothelial activation, inflammatory modulation, and growth factor signaling (Soumya and Sudhakaran, 2024; Wang et al., 2024).

In contrast, the absence of significant angiogenic effects observed for *Mauritia flexuosa* oil highlights the importance of phytochemical composition in determining biological activity. Oils rich in fatty acids and carotenoids, although possessing antioxidant properties, may not directly stimulate angiogenic signaling pathways. This interpretation is supported by studies demonstrating that certain compounds can even inhibit angiogenesis under specific conditions, particularly when oxidative stress pathways are activated (Jiao et al., 2017). Thus, the differential effects observed among the tested oils reinforce the concept that angiogenic modulation is highly dependent on chemical structure and bioactive composition.

Furthermore, the strong correlation observed between vascular endpoints and junctions supports the interpretation of a coordinated angiogenic response, involving both sprouting and network maturation. This pattern is characteristic of functional angiogenesis and has been previously described in experimental models evaluating vascular development.

From an ethnopharmacological perspective, the present findings provide experimental support for the traditional use of copaiba and jatobá in wound healing and tissue repair. These biological processes are intrinsically linked to angiogenesis, reinforcing the relevance of traditional knowledge as a guide for the selection of bioactive plant species.

Despite these promising findings, some limitations must be acknowledged. The chemical characterization of the oils was based on supplier information and literature data, without direct chromatographic validation. Additionally, the absence of molecular assays limits mechanistic interpretation. Future studies integrating GC–MS analysis and evaluation of angiogenic markers such as VEGF, FGF, and HIF-1 α are necessary to further elucidate the underlying mechanisms.

In conclusion, *Copaifera langsdorffii* and *Hymenaea courbaril* oils exhibit significant pro-angiogenic activity in the CAM model, supporting their traditional use and highlighting their potential as sources of bioactive compounds for regenerative medicine. These findings contribute to the growing evidence supporting the role of plant-derived substances in vascular modulation and tissue repair.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work, the authors used ChatGPT (OpenAI) to assist in language refinement and text structuring. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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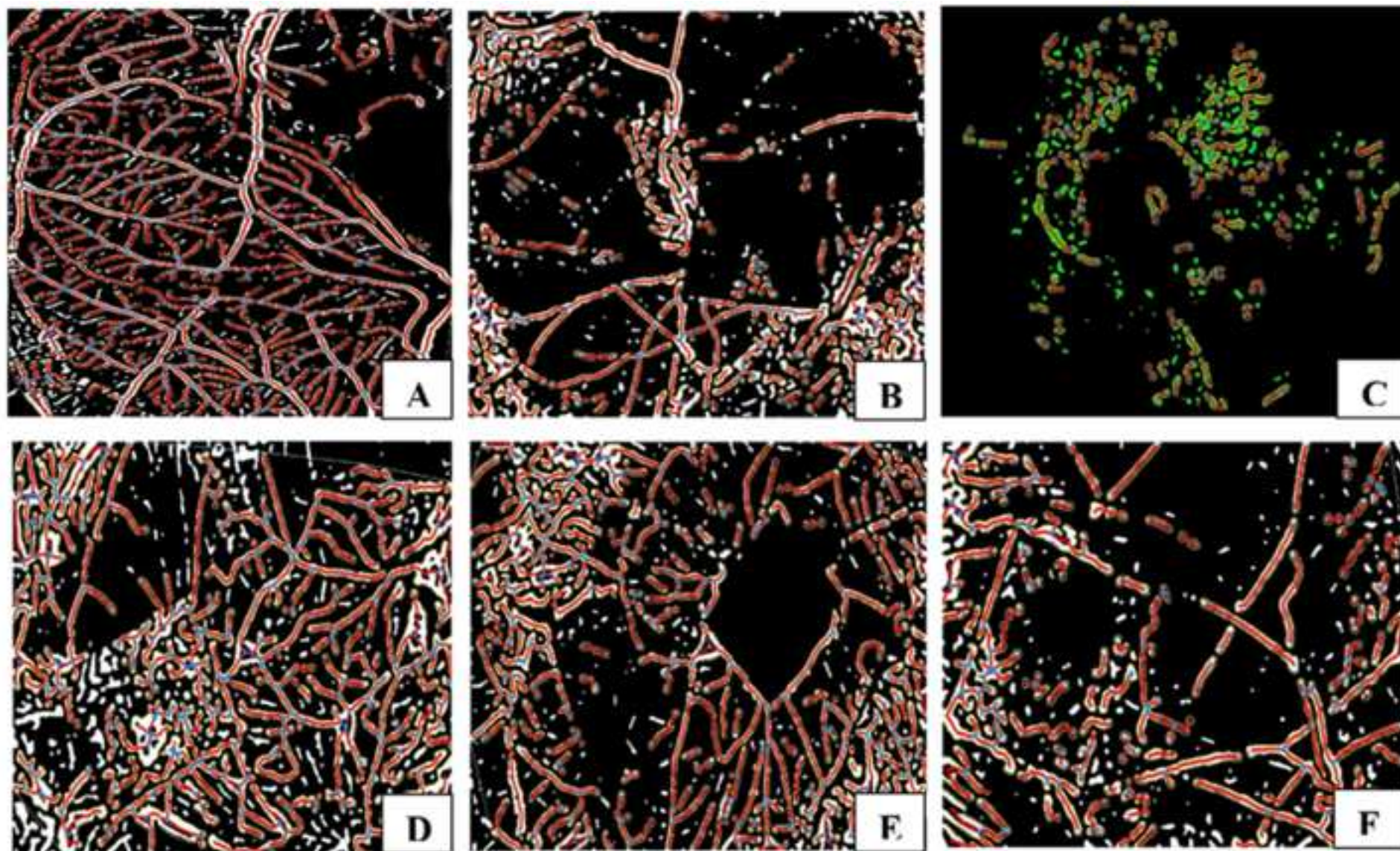
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Conflict of Interest

The authors have declared no conflict of interest

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