

REVIEWER'S REPORT

Manuscript No.: IJAR-59164

Title: Anti-inflammatory activity of aqueous extracts from the fruits of two tomato varieties cultivated in Cote d Ivoire

Recommendation:

Accept as it is

Accept after minor revision.....

Accept after major revision ...YES.....

Do not accept (*Reasons below*)

Rating	Excel.	Good	Fair	Poor
Originality		☐		
Techn. Quality			☐	
Clarity		☐		
Significance		☐		

Reviewer's ID: JPR- 094

Detailed Reviewer's Report

Reviewer Report

1. Overall assessment

The manuscript addresses an interesting and relevant topic: the evaluation of the anti-inflammatory potential of aqueous extracts prepared from two locally cultivated tomato varieties. The study has a potentially useful experimental concept because it compares **two tomato varieties, two extraction approaches (maceration and decoction), two doses, and an ibuprofen reference group** in an established acute inflammation model. The authors also included hematological parameters as an additional assessment.

The results indicate reduction of carrageenan-induced paw edema, particularly with the Locale Côtelette macerate, with reported inhibition exceeding 80% at one treatment condition.

However, several **methodological, statistical, ethical, scientific interpretation, and presentation issues** should be addressed before the manuscript can be considered for publication.

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2. Strengths of the manuscript

2.1 Relevant research topic

The anti-inflammatory potential of edible plant materials is an important area of pharmacological and nutritional research. The manuscript addresses the possibility of utilizing tomato-derived preparations as a source of bioactive compounds.

2.2 Comparison of two tomato varieties

The comparison between **Cobra F1** and **Locale Côtelette** is a useful feature because it allows the authors to examine whether biological activity differs between varieties. The manuscript clearly identifies the two varieties and their source.

2.3 Comparison of extraction methods

Both **maceration** and **decoction** were investigated. This provides an interesting experimental comparison because extraction conditions can influence the concentration and composition of plant constituents.

2.4 Inclusion of a reference drug

The use of **ibuprofen as a positive/reference control** is a strength because it provides a pharmacological comparator for interpreting the anti-inflammatory response.

2.5 Established experimental model

The carrageenan-induced rat paw edema model is a recognized experimental model for acute inflammation. The manuscript provides information regarding carrageenan concentration and administration.

2.6 Multiple treatment groups

The experiment includes different doses and extraction methods for both tomato varieties. This gives the study a comparative design rather than evaluating only one extract.

2.7 Hematological assessment

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Assessment of WBC, RBC, hemoglobin and platelet parameters provides additional information regarding the effects of treatment. The authors report that WBC and platelet values did not differ substantially from controls.

2.8 Clear biological signal

The reported reduction in edema is substantial for some treatment groups. In particular, Locale Côtelette macerate at 25 mg/kg showed a decrease in edema from 29.22% at 1 h to 9.39% at 3 h.

3. Weaknesses / Major concerns

3.1 *Ethical approval is not reported*

This is the **most important issue**.

The manuscript describes an experiment involving **50 Wistar rats**, including induction of inflammation and intraperitoneal administration of extracts.

However, there is no clearly reported:

- Institutional Animal Ethics Committee approval
- ethical approval/reference number
- animal welfare statement
- statement concerning applicable animal experimentation guidelines
- description of humane endpoints

Reviewer comment:

The authors should provide the relevant ethical approval number and identify the institutional committee that approved the animal experiment. A clear statement regarding compliance with applicable animal welfare guidelines is essential.

Without adequate ethical documentation, many journals may not consider the manuscript further.

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3.2 Sample size is very small

Each experimental group contains only **five animals (n=5)**.

Although n=5 may be used in exploratory animal studies, the manuscript does not provide:

- sample-size calculation
- power analysis
- effect-size justification

Reviewer comment:

The authors should justify the selected sample size, preferably with an a priori power calculation or an appropriate methodological justification.

3.3 Statistical analysis requires substantial improvement

The manuscript states that comparisons were performed using **Student's t-test**.

However, the experiment involves:

- multiple treatment groups,
- multiple doses,
- two extraction methods,
- two tomato varieties,
- repeated observations at 1, 2 and 3 h.

Using multiple independent t-tests creates a substantial risk of **type-I error inflation**.

Recommended approach:

Depending on the actual experimental design and whether measurements were repeated on the same animals, the authors should consider:

- one-way ANOVA with an appropriate post-hoc test, or
- two-way/mixed-effects ANOVA for treatment × time effects,

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- followed by an appropriate multiple-comparison correction.

Reviewer comment:

The statistical methodology should be reconsidered. The use of multiple Student's t-tests for numerous treatment comparisons and time points may inflate the probability of false-positive findings.

4. Important methodological concern: measurement of paw edema

The manuscript states that a digital caliper was used to measure paw edema.

However, the manuscript refers to “**paw volume**” while describing measurement using a caliper.

A caliper normally measures a **linear dimension**, whereas paw volume requires an appropriate volumetric method such as plethysmometry, unless the authors have specifically validated their calculation.

This needs clarification.

Reviewer comment:

The authors should clarify precisely how paw edema/volume was measured using a digital caliper and how the reported percentage increase was calculated. If paw volume was estimated from linear dimensions, the mathematical method and validation should be provided.

This is an important issue because it affects interpretation of the primary outcome.

5. Possible inconsistency in the calculation of edema

The manuscript defines:

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V_t = Paw volume of treated animal at time t

V_0 = Paw volume of the T0 control.

This requires clarification because in a standard carrageenan paw-edema experiment, the baseline value is generally the **same animal's pre-induction paw measurement**, rather than the paw measurement of a separate untreated control group.

Reviewer comment:

The authors should clarify whether V_0 represents the baseline paw measurement of the same animal before carrageenan administration or the measurement from the untreated control group. The current description may lead to ambiguity in the calculation.

6. Limited characterization of the tomato extracts

The manuscript attributes the activity to compounds such as **lycopene and polyphenols**, but no direct phytochemical characterization of the extracts appears to have been performed.

There is no reported:

- total phenolic content,
- total flavonoid content,
- lycopene quantification,
- HPLC/LC-MS analysis,
- chromatographic fingerprint,
- extract yield comparison.

Reviewer comment:

The mechanistic discussion should be presented more cautiously because the study did not directly quantify lycopene, polyphenols, flavonoids or other bioactive constituents in the tested extracts.

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7. Overinterpretation of the results

The manuscript concludes that regular consumption of these tomatoes could be a promising alternative for prevention of inflammatory diseases.

However, the experiment is an **acute animal inflammation study**, not a human clinical study.

Therefore, the findings cannot directly establish that eating these tomatoes will prevent inflammatory diseases in humans.

Reviewer recommendation:

Replace strong statements about prevention/treatment with wording such as:

“The findings provide preliminary experimental evidence supporting further investigation of the anti-inflammatory potential of these tomato extracts.”

8. Hematological results should not be interpreted as proof of safety

The authors describe the absence of major changes in WBC and platelet counts as evidence suggesting absence of immunotoxic effects.

However, hematological parameters alone cannot establish **overall safety or absence of immunotoxicity**.

No:

- serum biochemical parameters,
- liver-function markers,
- kidney-function markers,
- histopathology,
- organ-weight analysis,
- longer-term toxicity study

are presented.

Reviewer comment:

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The conclusion regarding “immunotoxicity” should be moderated. Hematological measurements provide limited safety information and should not be presented as a comprehensive toxicity assessment.

9. The discussion is longer than necessary and sometimes speculative

The discussion contains extensive explanations of NF- κ B, COX-2, AMPK, JAK/STAT3, MAPK, cytokines and iron metabolism.

Some of these mechanisms were **not measured experimentally in the present study.**

For example, the authors did not measure:

- NF- κ B,
- TNF- α ,
- IL-1 β ,
- IL-6,
- IL-8,
- COX-2,
- AMPK,
- JAK/STAT3,
- MAPK.

Reviewer comment:

The mechanistic discussion should distinguish clearly between mechanisms demonstrated by the present experiment and mechanisms proposed based on previous literature.

10. The statement regarding anemia prevention is not adequately supported

The manuscript suggests that increases in RBC and hemoglobin indicate that tomato consumption could help prevent iron deficiency and anemia.

This conclusion is too strong based on the presented experiment.

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The study did not measure:

- serum iron,
- ferritin,
- transferrin,
- total iron-binding capacity,
- dietary iron status
- iron absorption.

Reviewer comment:

The claim concerning prevention of iron-deficiency anemia should either be removed or substantially moderated because the present experiment was not designed to investigate iron metabolism or anemia prevention.

11. Novelty should be better established

The manuscript presents the work as an investigation of two tomato varieties cultivated in Côte d'Ivoire. However, tomato extracts and their anti-inflammatory properties have previously been investigated.

The authors should clearly explain:

What is new about this study?

For example:

- Are these specific tomato varieties previously unstudied?
- Is the comparison between maceration and decoction novel?
- Is the combination of variety × extraction method × dose novel?
- Are there specific local agricultural or nutritional implications?

12. Reference quality and consistency need improvement

The reference list contains a mixture of:

International Journal of Advanced Research

Publisher's Name: Jana Publication and Research LLP

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- journal articles,
- doctoral dissertations,
- master's theses,
- general sources.

Several references require verification of complete bibliographic information and DOI details.

For example, some entries appear incomplete or inconsistently formatted.

Reviewer comment:

The reference list should be carefully checked against the journal's reference style. DOI, volume, issue, page/article number and publisher information should be provided where applicable.

13. Language and presentation require substantial editing

There are numerous grammatical and typographical problems, including:

- “Lycopersiconesculentum” formatting,
- inconsistent spacing,
- “Anti-inflammatory”/“anti inflammatory” inconsistencies,
- “Technicalequipment,”
- “Statisticalanalysis,”
- “Meanweight,”
- “P a g e” formatting,
- inconsistent use of *Côtelette*/Cotelette,
- “Rattus norvegicus” in the figure caption.

These issues reduce the professional quality of the manuscript.

Reviewer comment:

The manuscript requires comprehensive English language editing and technical formatting before publication.

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14. Key scientific points that should be highlighted

Key Point 1

The study provides comparative evidence that aqueous extracts of two tomato varieties can reduce experimentally induced acute inflammation in rats.

Key Point 2

The response varies according to:

- tomato variety,
- extraction method,
- dose,
- observation time.

Key Point 3

The Locale Côtelette macerate at 25 mg/kg produced a particularly marked reduction in paw edema.

Key Point 4

The study includes both a negative control and ibuprofen reference group, strengthening the experimental comparison.

Key Point 5

The work is preliminary and should be regarded as **preclinical evidence**, rather than evidence of clinical efficacy.

15. Significance of the study

The study has potential significance because it investigates an **edible and commonly available plant material** rather than a synthetic compound and compares locally cultivated tomato varieties.

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The most scientifically relevant contribution is the comparison of **variety + extraction procedure + dose** within the same experimental model.

The findings could justify future work involving:

- phytochemical profiling,
 - quantification of lycopene and phenolic constituents,
 - dose-response studies,
 - larger animal studies,
 - additional inflammatory biomarkers,
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- histopathological evaluation,
 - chronic toxicity studies,
 - eventually, appropriately designed human studies.

The current findings should therefore be described as **preliminary experimental evidence** rather than clinical evidence.

16. Recommended major revisions

No.	Issue	Priority
1	Animal ethical approval and approval number	Critical
2	Clarification/validation of paw edema measurement	Critical
3	Clarification of baseline/control calculation	Critical
4	Reassessment of statistical methodology	Major
5	Justification of n=5 sample size	Major
6	Reduce unsupported mechanistic claims	Major
7	Moderate safety/immunotoxicity claims	Major
8	Moderate claims regarding anemia prevention	Major
9	Strengthen novelty statement	Major

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No.	Issue	Priority
10	Improve references	Minor–Major
11	Professional English editing	Major
12	Improve figures/tables and terminology	Major

17. Recommendation to the Editor

Recommendation: MAJOR REVISION

Reviewer recommendation:

The manuscript addresses a relevant topic and presents potentially interesting preliminary findings concerning the anti-inflammatory activity of aqueous extracts from two tomato varieties cultivated in Côte d'Ivoire. The comparative design involving two varieties, two extraction procedures, different doses and an ibuprofen reference group is a strength. However, important methodological and interpretative issues need to be addressed, particularly regarding animal ethical approval, measurement and calculation of paw edema, statistical analysis, sample-size justification, extract characterization and the extent of the conclusions. The manuscript also requires substantial language and formatting revision. Therefore, I recommend **Major Revision**. If the authors adequately address the methodological concerns and moderate unsupported conclusions, the manuscript may be reconsidered for publication.

Overall reviewer view

Scientific interest: Good

Novelty: Potentially interesting but needs stronger justification

Experimental design: Reasonable but requires clarification

Statistical analysis: Requires revision

Methodological reporting: Insufficient in important areas

Interpretation: Some overstatement

Presentation: Requires substantial language editing

Significance: Potentially useful preliminary/preclinical study

Recommendation: MAJOR REVISION

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