



PEER-REVIEW REPORT

Name of journal: *World Journal of Experimental Medicine*

Manuscript NO: 110757

Title: Ferula Assafoetida Induced Colon Cancer Cells Differentiation Through JNK/MAPK Signalling Pathway Activation

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 08436563

Position: Peer Reviewer

Academic degree and professional title: Senior Researcher, Senior Scientist

Reviewer’s Country/Territory: Bangladesh

Author’s Country/Territory: Egypt

Manuscript submission date: 2025-06-13

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2025-06-24 18:58

Reviewer performed review: 2025-06-30 11:17

Review time: 5 Days and 16 Hours

Content to be reviewed	<p>Does the manuscript’s content fall within the scope of the journal? Yes</p> <p>Is there any Key Word that is not included in the manuscript title? Yes</p> <p>Do authors’ affiliations correspond to the content of the manuscript? Yes</p> <p>Does the Abstract contain the contents of each part of the manuscript (IMRaD)? No</p> <p>Are the Key Words complete? Yes</p>
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Is the content of the Introduction adequate? **No**
Is the content of the Materials and Methods complete?
No
Is the description of the experiments clear and
complete? **No**
Are the experimental data presented in the
manuscript's biostatistics content reliable? **No**
Are the experimental data of the Results true and
reliable? **No**
Are the quality and resolution of the images up to
standard? **No**
Do the selection and design of the figures and tables
follow the principles of necessity and clarity? **No**
Is there any duplication between various parts of the
manuscript and between the main text and the content
presented in the figures and tables? **No**
Are the figures and tables numbered consecutively in
the order in which they appear in the manuscript? **No**
Is the content of the Discussion reasonable? **No**
Is the Conclusion reasonable? **No**
Are all references necessary and reasonable? **Yes**
Do authors omit important references? **No**
Are all references related to the topic of the
manuscript? **Yes**
Do authors only cite their own earlier publications? **No**
Is the manuscript's text correct, concise, and clear? **No**
Will the manuscript's content be of interest to readers?
No
Are additional experiments needed for the study? **No**
Does the research scope comply with ethics? **Not**



	Applicable
Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	No
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Major revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	

SPECIFIC COMMENTS TO AUTHORS

The manuscript presents a well-designed study investigating the potential of Ferula Assafoetida (F. Assafoetida) as a differentiating agent for colon cancer cells via the JNK/MAPK pathway. The work is scientifically sound, with robust methodologies and clear results. However, some areas require clarification, refinement, or expansion to enhance the manuscript's impact and readability. Below are specific comments and recommendations.



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1. Novelty and Contextualization

- The introduction adequately reviews CRC and the role of differentiation but could better highlight the novelty of using *F. Assafoetida* in this context. Compare with existing literature on other natural compounds (e.g., curcumin, resveratrol) to underscore *F. Assafoetida*'s unique advantages.
- Clarify why *F. Assafoetida* was chosen over other phytochemicals with known differentiation-inducing properties (e.g., butyrate analogues).

2. Mechanistic Depth

- The study focuses on JNK/MAPK activation but does not explore crosstalk with other pathways (e.g., Wnt/ β -catenin, PI3K/AKT). Include a discussion on how JNK/MAPK might interact with these pathways to drive differentiation.
- Provide Western blot or immunofluorescence data to corroborate qPCR results for JNK/MAPK protein expression/phosphorylation.

3. Dosage and Pharmacokinetics

- Justify the chosen doses of *F. Assafoetida* (e.g., 343.6 μ g/mL) and NaBT (3.3 mg/mL). Are these concentrations physiologically relevant? Compare with prior *in vivo* or clinical studies.
- Include a brief discussion on bioavailability and potential toxicity of *F. Assafoetida* in humans.

4. Figures and Data Presentation

- Figure 1A: Label axes clearly (e.g., "Cell Viability (%)" vs. "Concentration (μ g/mL)"). Include error bars for triplicate experiments.
- Figure 2/3: Merge cell cycle and apoptosis data into a single figure for coherence. Use color to distinguish treatment groups.
- Figure 4C: Ensure DNA laddering gels are high-resolution and include molecular weight markers. Annotate lanes clearly (e.g., "1/4 IC₅₀", "Control").



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5. Statistical Analysis

- Specify the number of replicates for each experiment (e.g., $n = 3$ biological replicates).
- For ANOVA results, report F-values and degrees of freedom alongside p-values.

6. Abstract

- Replace "king unit/mL" with standard units (e.g., U/mL or IU/mL) for ALP activity.
- Clarify whether the "complete DNA degradation" observed was dose-dependent (mentioned in Results but not Abstract).

7. Methods

- GC-MS: Specify the database used for compound identification (e.g., NIST).
- qRT-PCR: Include primer efficiencies and melting curves to validate specificity.

8. Results

- Table 1: Use consistent units (e.g., % vs. g/100g for phenolic/flavonoid content).
- Table 2: Define ">4n" (polyploid cells?) in the legend.

9. Discussion

- Contrast the efficacy of F. Assafoetida with NaBT more critically. Why is F. Assafoetida superior despite NaBT's established role in differentiation?
- Address limitations (e.g., lack of in vivo validation, single cell line used).

10. Language and Clarity

- Correct minor grammatical errors (e.g., "revealed by the significant increase" → "revealed a significant increase").
- Avoid redundant phrases (e.g., "untreated control cells" → "controls").
- Enhanced mechanistic insights (pathway crosstalk, protein-level validation).
- Improved figure quality and labeling.
- Justification of experimental doses and pharmacokinetic relevance.
- Clarification of novelty relative to existing literature.



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- Ensure all figures are cited in the text (e.g., Figure 1B is mentioned but not shown in the provided content).
- Verify that supplementary data (e.g., GC-MS raw files) are available upon request.