LIFE Science Hub
JOURNAL OF SCIENCE
EXPANDING KNOWLEDGE ABOUT NUTRITION AND HEALTH

ORIGINAL RESEARCH
Volume 1, Issue 4, November 2026
ISSN 2845-7501

Cytotoxicity of cinnamaldehyde, carvacrol, and eugenol: a cellular comparison

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1. ABSTRACT

The study compared three plant-derived aromatic compounds in both cancer cells and normal cells. The results indicate that trans-cinnamaldehyde and carvacrol can reduce the viability of both cell types under laboratory conditions, while eugenol showed a different behavior. These are not clinical data.The authors' summary describes an in vitro experiment, meaning it was conducted on cells maintained in a laboratory. Ranjitkar and colleagues exposed HeLa cells, a cell line derived from cervical cancer, and human skin fibroblasts (CCD-1123Sk), which are normal connective tissue cells, to trans-cinnamaldehyde, carvacrol, and eugenol. After 24 hours, trans-cinnamaldehyde and carvacrol reduced cell viability by more than half at 100 µg/mL in both models. Eugenol did not produce the same effect until reaching 400 µg/mL. With 100 µg/mL of trans-cinnamaldehyde, the researchers observed cell detachment and an increase in apoptosis, or programmed cell death, in both the HeLa cells and the fibroblasts. Gene expression analysis did not reveal significant changes in most of the genes examined, including BCL2, CASP3, CASP8, MLKL, RIPK1, and RIPK3. The exception involved the HeLa cells treated with eugenol. The main takeaway is one of caution: in this model, the reduction in viability did not appear to be selective for cancer cells. The work does not demonstrate anti-cancer effects in the body, nor does it describe the effects of cinnamon consumed as a spice.

ONLINE ARTICLE

ARTICLE INFORMATION

Published: November 18, 2026
Updated: November 18, 2026

KEYWORDS

cinnamaldeide e eugenolo tossicità cellulare
trans-cinnamaldeide cellule tumorali
eugenolo fibroblasti normali
carvacrolo citotossicità in vitro
composti aromatici e cellule
fitocomplesso e cellule tumorali

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Through articles, reviews, in-depth analyses and expert contributions, the Journal champions evidence-based medicine and science, fostering a correct interpretation of scientific data and countering misinformation. Every piece of content is developed with the aim of translating the complexity of research into understandable, useful and applicable information, while keeping intact the principles of accuracy, transparency and scientific independence.

Free from political, industrial and commercial influence, the journal stands as an authoritative and independent editorial space, dedicated to promoting scientific culture, professional development and the growth of health awareness among the public.

2. WHAT THIS RESEARCH ANALYZED

The study investigated whether certain plant-derived aromatic compounds could damage cancer cells more easily than non-cancerous cells. To verify this, Ranjitkar and colleagues used two human cell culture models: HeLa cells and CCD-1123Sk fibroblasts. HeLa cells are cancer cells frequently used in research, while fibroblasts produce connective tissue components and were used as a non-cancerous comparison.The researchers tested trans-cinnamaldehyde, carvacrol, and eugenol for 24 hours. They measured metabolic viability using the MTT assay, membrane damage with the LDH assay, apoptosis via flow cytometry, and several messenger RNAs using RT-qPCR, a technique that quantifies the activity of specific genes. The study design therefore allows for the observation of direct cellular signals, but it cannot predict safety or benefits in humans.

3. WHAT RESULTS EMERGE FROM THE STUDY

The clearest result is that, under the conditions tested, trans-cinnamaldehyde and carvacrol did not show clear selectivity for HeLa cells. At 100 µg/mL, both reduced the viability of both tumor cells and fibroblasts by more than 50% after 24 hours. Simply put, the observed damage was not confined to the tumor model.Trans-cinnamaldehyde at 100 µg/mL also increased the number of cells with characteristics compatible with apoptosis after four hours in both cell types. However, genes linked to apoptosis and regulated necrosis did not change in a statistically significant way in most comparisons. Eugenol proved different: up to 400 µg/mL, it did not reduce viability to a comparable extent; in HeLa cells, it modified BCL2, MLKL, and RIPK1. This finding does not define a complete mechanism and does not equate to a therapeutic effect.

4. WHY THIS STUDY IS RELEVANT

This work is relevant because it separates two questions that are often confused: a molecule may be toxic to cells in culture, but that does not mean it is a selective treatment against a tumor. In the model examined, trans-cinnamaldehyde also affected non-tumor fibroblasts. This highlights the importance of evaluating efficacy and potential cellular damage together.It is also useful for understanding why the behavior of a single pure compound cannot be attributed to whole cinnamon. Trans-cinnamaldehyde was studied in isolation; carvacrol and eugenol come primarily from other plant sources. Concentration, solvent, duration of exposure, and cell type profoundly change the result. For this reason, the work provides information on experimental cell biology, not on the dietary use of the spice.

5. STUDY LIMITATIONS AND WHAT IT DOES NOT DEMONSTRATE

This is a study on two cell lines, not a clinical trial, an animal study, or an analysis of dietary cinnamon. Absorption, metabolism, tissue distribution, elimination, or tolerability in the body were not evaluated. The concentrations applied directly to the cells are not automatically achievable after consuming food.The comparison includes only one tumor model and one non-tumor model. HeLa cells and fibroblasts do not represent all cancers or all healthy tissues. Furthermore, the reduction in viability detected by the tests does not, on its own, clarify which biological pathway prevails. The study by Ranjitkar and colleagues does not prove that trans-cinnamaldehyde, carvacrol, or eugenol prevent, treat, or worsen cancer in humans.

6. INDEPENDENT SUPPORTING EVIDENCE

A first converging element concerns the difference between a plant matrix and an isolated molecule. Singh and colleagues compared an aqueous extract of *Cinnamomum zeylanicum* and commercial cinnamaldehyde in various tumor cell lines, murine cells, and primary cells. At a concentration of approximately 10.24 µM of cinnamaldehyde, the extract inhibited the growth of many tumor models by 35% to 85%, while isolated cinnamaldehyde at 10 µM had a limited effect. This indirectly supports the idea that the behavior of a matrix does not coincide with that of the pure substance, but it does not demonstrate synergy nor an effect in humans [1].In a second study, an extract rich in trans-cinnamaldehyde reduced the viability of HCT 116 and HT-29 colon cancer cells and showed signals compatible with cell cycle arrest and apoptosis. The model included two tumor lines, without a comparison with normal cells; it therefore only confirms that preparations rich in

cinnamaldehyde can be cytotoxic in specific cultures [2]. Varadarajan and colleagues also observed apoptosis and arrest in the S phase, i.e., in the DNA replication phase, in SCC-25 oral carcinoma cells treated with extracts and isolated compounds. The confirmation remains preclinical and indirect with respect to the selectivity evaluated by Ranjitkar [3].

7. CONFLICTING EVIDENCE

The results on eugenol show how much the experimental context can change the outcome. Slamenová and colleagues studied eugenol in HepG2 hepatoma cells, Caco-2 colon cancer cells, and VH10 human fibroblasts. Eugenol was found to be cytotoxic in all three models and increased DNA breaks in VH10 fibroblasts at the concentrations examined. This is consistent with the caution in Ranjitkar's study, but contrasts with the absence of a relevant effect of eugenol under his experimental conditions [4].Conversely, Issa and colleagues reported that eugenol reduced proliferation and colony formation in two oral carcinoma lines more than in the control non-tumor epithelial cells. The study, based on three cell models and four independent experiments, suggests a possible selectivity dependent on tissue, dose, and cell line [5]. No directly conflicting evidence sufficiently relevant beyond these model-dependent results has been identified; this does not prove the absence of contrary findings.

8. QUADRO COMPARATIVO E SINTESI DELLE EVIDENZE

Comparison between independent publications and the work of Ranjitkar and colleagues.

Quadro comparativo

Publication	Model and main result	Relation to the study	Main limitation
Singh et al., 2009 [1]	Aqueous extract and cinnamaldehyde in tumor lines, murine and primary cells; different response between extract and isolated compound.	Indirect confirmation of the relevance of the matrix.	Cell cultures only; mechanism not demonstrated.
Kim et al., 2023 [2]	Cinnamaldehyde-rich extract in HCT 116 and HT-29; reduction in viability and signs of apoptosis.	Confirms cytotoxicity in other tumor models.	Lacks a comparison with non-tumor cells.
Varadarajan et al., 2020 [3]	Extracts and isolated compounds in SCC-25; apoptosis and S-phase arrest.	Confirms model-dependent cellular activity.	Single tumor line; no clinical data.
Slamenová et al., 2009 [4]	Eugenol in HepG2, Caco-2, and VH10 fibroblasts; cytotoxicity and DNA damage in fibroblasts.	Shows different outcomes for eugenol and potential damage to non-tumor cells.	In vitro experiment, without clinical comparison.
Issa et al., 2024 [5]	Eugenol in oral carcinomas and non-tumor epithelial cells; greater cytotoxicity in tumor models.	Indicates possible selectivity in a different context.	Results limited to oral cell lines.

9. SINTESI EDITORIALE E CONCLUSIONI

EDITORIAL CONCLUSION

The study by Ranjitkar and colleagues compared trans-cinnamaldehyde, carvacrol, and eugenol in HeLa tumor cells and non-tumor skin fibroblasts. Trans-cinnamaldehyde and carvacrol reduced the viability of both models, while eugenol did not show the same effect under the tested conditions. The essential point is that a reduction in cell viability does not equate to a selective action against a tumor. Independent publications confirm that cinnamon extracts, cinnamaldehyde, and eugenol can produce different effects depending on composition, dose, duration of exposure, and cell type. Some studies suggest a higher sensitivity in specific tumor lines; others document effects on non-tumor cells as well. Overall, the literature supports the experimental interest in these compounds, but it does not allow for the translation of these data into the prevention or treatment of cancer in humans. Dietary cinnamon, an extract, and a pure molecule remain distinct objects of study.

Aggiornato al 24/11/2026. Questo contenuto riflette una sintesi divulgativa delle evidenze scientifiche al momento della pubblicazione e non sostituisce il parere medico.

10. TRANSPARENCY AND SCIENTIFIC RESPONSIBILITY

Artificial Intelligence was used solely as a tool for editorial and documentary support. All content, interpretations, bibliographic citations and conclusions have been verified, reviewed and approved by the author, who assumes full scientific responsibility for them.

The manuscript was also subjected to independent peer review prior to publication.

To ensure the greatest transparency, the complete history of the article, including the dates of submission, revision, acceptance and publication, as well as information on the peer review process, is available on the dedicated Article History page.

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