

Review of: "Developing the theory of Toxic Chemotherapeutic Nutrition for Cancer Cells: Glucosodiene Polymer Structure, Safety, Efficacy, and Human Outcomes in Targeting Tumors via Glucose Mutation"

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Potential competing interests: No potential competing interests to declare.

The article defends a theory of potential clinical interest for cancer patients. However, the figure legends need to be much more detailed to be complete and understandable. Details of clinical trials are missing. Figures 14 and 15 are not convincing. Paragraphs 7 and 8 are too speculative to be included in a scientific article unless additional scientific data on the mechanism of action can be provided.

In conclusion, I suggest reconsidering a revised version taking into account the following main points:

1. Figure 2:

The graphics are blurred and should be improved.

Legend needs improvement:

- Can the authors define the following abbreviations: a-KG, HIF, 3PG, AKT, PI3K, TCA, NADH?
- Can the authors clearly/fully describe the figure?
- It is stated that glycolysis involves the generation of NADH, whereas NADH is not mentioned in the figure. Can the authors include NADH within the figure?

2. Paragraph 5:

Please correct 10x103 cells/well by 10x10³ cells/well.

Please define SPSS.

Fibroblasts are support cells that are highly resistant to various treatments. Can the authors provide data with much more fragile cells such as epithelial cells?

When comparing figure 13 to figure 12, it appears that exposure to glucosodiene, may have an impact on cell proliferation: can the authors provide cell counts? Can the authors provide evidence that glucosodiene has no impact on the cell phenotype (study of cell morphology by staining plasma membrane and/or of cortical actin).

3. Paragraph 6:

Can the authors provide more information about how patients were treated: doses, frequency of administration, administration route...

Figures 14 and 15 should be combined into a single figure with a higher and identical resolution to facilitate comparison of the images. Can the authors describe the figures clearly and indicate what should be seen, as it is not clear to me that glucosodiene treatment is beneficial to the patient. Furthermore, it is stated that glucosodiene has no toxicity although it seems that the patient lost a lot of weight after only 15 days of treatment. Can the authors comment on this particular point? Can the authors provide information about how toxicity was evaluated?

Are the authors able to provide additional data from other patients?

4. Paragraph 7 is highly speculative. Can the authors provide data on the affinity of glucosodiene for the different GLUT receptors? Do the authors have any evidence that glucosodiene impacts AKT and ERK kinases or any other signaling pathways, including those leading to cell growth arrest, programmed cell death or cytokine production? If not, this paragraph is not relevant and should be deleted.

5. Paragraph 8 is redundant with paragraph 7 and, like paragraph 7, is highly speculative. Unless evidence of the mechanism involved is provided, I suggest deleting this section while stating that the mechanisms involved are as yet unknown.