

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 concept of influencing the enhanced metabolic state of cancer cells discussed in the Article is interesting in general as it can serve as a promising strategy to reduce tumor growth and progression. However, in the particular case of Glucosodiene, the Authors do not provide enough evidence on both its efficacy and safety.

- 1. The efficacy of the agent must be supported by the data on different levels, both in vitro and in vivo. If the authors indicate that Glucosodiene reduces cancer cell growth by altering their metabolic activity, they have to perform an in vitro study applying cancer cell lines both to demonstrate the ability of the compound to reduce their growth/migration potential and to provide mechanistic explanations of its action. In the next step, the authors should conduct in vivo studies applying transplantable rodent tumor models to support the efficiency of Glucosodiene.
- 2. The safety is the main issue. Glucose (and Glucosodiene as its modification) is not specific enough to perform targeted action on tumor cells. Affecting such a general metabolic pathway would undoubtedly be extremely toxic for all the tissues of the body. Even in case the general toxicity of Glucosodiene is not very high, more or less long-term treatment should result in altered glucose metabolism in normal tissues leading to metabolic complications such as insulin resistance, T2D, etc. In vitro study on a normal fibroblast cell line only indicates the absence of acute cytotoxicity but is not sufficient to reveal any issues connected with the altered metabolic state. The authors should study the specific safety both in vitro and in vivo, and also think about the targeted delivery of the compound to the tumor.

In conclusion, before its use in clinics, Glucosodiene is supposed to undergo the full spectrum of comprehensive fundamental research and preclinical studies, with justification on mechanism of action, in vitro and in vivo efficacy, and safety. To date, even the proposed mechanism of Glucosodiene action is not supported by enough amount of data. As in vivo studies are complicated and time-/cost-intensive, I'd recommend the Authors start with in vitro PoC experiments to support their hypothesis.

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