Investigation of antitumor effects of a sodium–glucose cotransporter-2 (SGLT-2) inhibitor for the treatment of prostate cancer (PCa).

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Background

Prostate cancer (PCa) is the second most common malignancy among men worldwide. A hallmark of PCa is metabolic reprogramming, characterized by increased glucose uptake to support rapid tumor growth. Sodium–glucose cotransporter-2 (SGLT-2) inhibitors are a relatively new class of antidiabetic agents that have demonstrated antitumor effects by disrupting glucose uptake and cellular energetics in various tumor models. By lowering glucose and insulin levels, improving insulin sensitivity, and reducing chronic inflammation, these agents create a metabolically unfavorable environment for tumor progression.

Objective(s)

This study aimed to evaluate the antitumor potential of canagliflozin, an SGLT-2 inhibitor in PCa.

Disclosure

The authors declare no conflicts of interest.

Methods

Androgen dependent (LNCaP) and independent (DU145 and PC-3) cells were cultured in RPMI media and allowed to adhere to the plates for 24 hours. They were then exposed to increasing concentrations of canagliflozin (10–50 µM) for 72 hours. Cell viability was then assessed using the MTS assay, which estimates the number of viable cells based on the biochemical reduction of a tetrazolium compound into a colored product by metabolically active cells. Finally, cells were incubated at 37 °C for approximately 2 hours, and absorbance was measured at 490 nm using a SpectraMax190® M-Series.

Discussion

These findings support repurposing SGLT-2 inhibitors, particularly in patients with type 2 diabetes, where metabolic modulation may offer dual therapeutic benefits. Future studies will investigate underlying mechanisms, including apoptosis, cell cycle regulation, inhibition of glucose uptake, and tumor invasiveness and migration. Translational efforts will focus on validating these effects in vivo using PCa xenograft models and exploring combinations with standard-of-care therapies.

Results / Conclusion

This study demonstrates that SGLT-2 inhibition with canagliflozin significantly reduces viability in both androgen-dependent and androgen-independent PCa cell lines, underscoring its potential applicability across distinct clinical stages of the disease.

Reference(s)

- Lin, Y., Zhang, Y., Wang, S., Cao, L., Zhao, R., Ma, X., Yang, Q., Zhang, L., & Yang, Q. (2024). Pharmacological targets of SGLT2 inhibition on prostate cancer mediated by circulating metabolites: A drug-target Mendelian randomization study. Frontiers in Pharmacology, 15, 1443045. https://doi.org/10.3389/fphar.2024.1443045

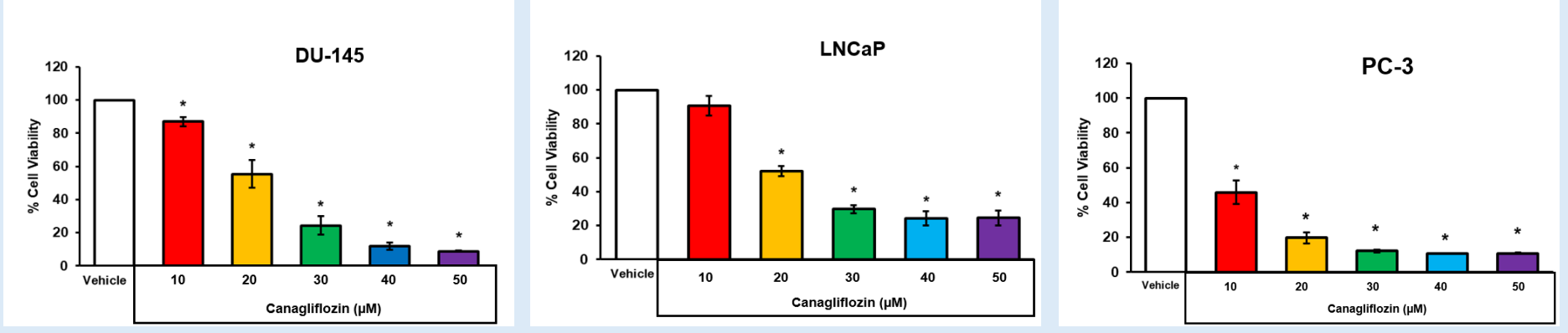

Fig.1: Canagliflozin inhibits DU145, LNCaP and PC-3 cell viability in a dose dependent manner. Results indicate Mean ± SE of three experiments. * Statistical significance (*p<0.05) in comparison to vehicle (DMSO) treated cells.