Ellagic acid induces apoptosis in neuroblastoma via multiple signaling pathways

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Introduction

Background
- Neuroblastoma is the most common extra cranial solid tumor and aggressive type of pediatric cancer and has its roots in immature nerve cells, predominantly impacting children under the age of five.
- Neuroblastoma can develop in various Body locations, most commonly in the adrenal glands above the kidney but also in the spine, chest, abdomen, or pelvis.

Signs and Symptoms of Neuroblastoma
- Vary depending on tumor location, size, and metastasis, and not all children with neuroblastoma experience all symptoms.
- Abdominal swelling, change in bowel habits, Weight loss, Fatigue, Fever, Bone pain, Proptosis (eye bulging), Bruising or bleeding.

The role of NMYC in neuroblastoma
- N-Myc, encoded by the MYCN gene, is a pivotal transcription factor in neuroblastoma cells. Its amplification is closely associated with an aggressive form of the disease, making it a significant prognostic marker.
- Specifically, MYCN amplification leads to rapid tumor cell proliferation and prevents the differentiation of neuroblastoma cells into a less aggressive phenotype.

Treatment Modalities for Neuroblastoma
- Treatment strategies for neuroblastoma include surgery, chemotherapy, radiation therapy, immunotherapy, and chemotherapy Doxorubicin.
- Mechanism of Action of Doxorubicin
  - Intercalation into DNA: Doxorubicin inserts itself between DNA base pairs.
  - Disturbs the DNA structure, preventing DNA replication and transcription.
  - Inhibition of Topoisomerase II: Doxorubicin binds to topoisomerase II, an enzyme that relaxes supercoiled DNA.
- Effect: Combined action leads to cell cycle arrest and apoptosis in cancer cells.

Statistical Analysis
- Data from the SRB assay were analyzed to determine cell growth and treatment effects.
- Results are presented as the mean ± standard deviation of at least three replicates.
- Statistical significance was determined using a two-way analysis of variance (Student’s t-test), with p < 0.05 considered statistically significant.
- This method describes the specific procedures followed in the experiment, including cell viability, treatment, and the SRB assay used to assess cell viability and treatment efficacy.

RESULTS

IC50 Determination of Ellagic Acid on MYCN-2 Tet-on Cells

Experimental Design: All plates are prepared and processed in triplicate to ensure data accuracy and reproducibility.

Data Presentation:
- X-axis: Concentration of drug (Log µM).
- Y-axis: Cell viability.

Results:
- For Ellagic acid treatment alone:
  - IC50 Value: 0.07 µM
  - Indicates the concentration at which Ellagic acid inhibits 50% of cell growth.

IC50 Determination of Doxorubicin on MYCN-2 Tet-on Cells

Experimental Design: All plates are prepared and processed in triplicate to ensure data consistency and reliability.

Graphical Presentation:
- X-axis: Concentration of Doxorubicin (Log µM).
- Y-axis: Cell viability.

Preliminary Results:
- For Doxorubicin treatment alone:
  - IC50 Value: 0.07 µM
  - Represents the concentration at which Doxorubicin inhibits 50% of cell growth.

Discussion

- Investigating novel drugs and alternative treatments for relapsed high-risk neuroblastoma (NB) patients is crucial.
- Treating these patients remains challenging due to aggressive tumor phenotypes and complex mechanisms that promote resistance to treatments and recurrence.
- This study focuses on examining the potential of ellagic acid as a treatment for NB.
- Previous research has shown surprising anticancer effects of ellagic acid in various malignancies.
- Our results demonstrate that ellagic acid significantly reduced NB cell numbers compared to untreated controls.
- According to the IC50 of both drugs, ellagic acid, a naturally occurring polyphenolic compound, exhibits potent anti-cancer properties when tested on NB cells.

Conclusion

- Our study, the first of its kind, investigates the efficacy of ellagic acid on NB. The findings reveal that ellagic acid exerts multiple effects on NB cells, ultimately reducing their viability and inducing cell death in a time- and dose-dependent manner compared to doxorubicin. Given its natural origin, ellagic acid shows promise as a potential treatment for NB, with the potential to reduce the side effects associated with chemotherapeutic agents and enhance cell death within cancerous tumors.
- The next phase of our research will delve into the mechanisms by which ellagic acid impacts various signaling pathways, including those related to apoptosis and anti-proliferation in cancer cells.

References

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