A polyphenolic plant flavonoid luteolin potentiates the growth inhibitory effects of erlotinib glioblastoma cell lines.

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Background

The GLOBOCAN reports of 2020 estimated 19.3 million new cases of cancer and estimated about 10 million cancer deaths.[1]

Among all cancer cases, brain and nervous system tumors account for 1.3%. In the US, glioblastoma multiforme (GBM) has an incidence rate of 4.32 per 100,000 people.[2]

The current therapeutic approach for GBM includes surgical resection, radiotherapy, and chemotherapy with temozolomide (TMZ).[3,4]

Luteolin is a common flavonoid that displays various beneficial effects such as antioxidant, anticancer, anti-inflammatory, and antiviral properties[5].

Erlotinib is an EGFR tyrosine kinase inhibitor that prevents intracellular phosphorylation of EGFR in cancer cells[6].

Objectives

To determine the antiproliferative and apoptotic effects of luteolin and erlotinib in glioblastoma cell lines, with the goal of also determining the key signaling pathways affected by these drug combinations

Methodology

Material and Assays

- Cell Lines: U87, U87 EGFR vIII and U251, U251 EGFR vIII cell lines
- Cell proliferation Studies - MTT Assay[5]
- Measurement and detection of LDH[6]
- Western Blot Analysis-cellular and apoptotic signaling[6]
- Caspase Assay[5]
- Apoptotic markers: PARP, Bcl-xL[6]

Statistical Analysis

- Data are presented as the mean ± standard error. Differences between the groups were tested using one-way ANOVA, followed by a Bonferroni post hoc test (α = 0.05). Statistical data analysis was conducted using GraphPad Prism 7 (San Diego, CA).

Results

Figure 1. Structures of Luteolin and Erlotinib

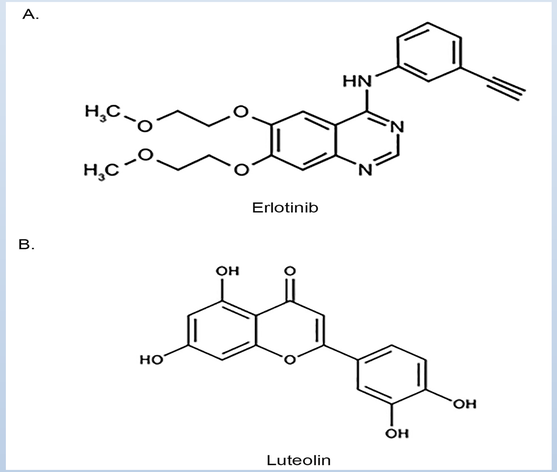


Figure 2. Effect of Luteolin and Erlotinib on GBM Cell Proliferation

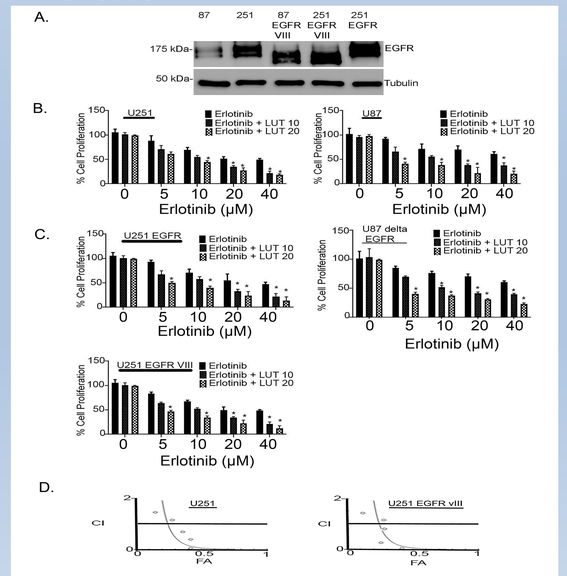


Figure 3. Effect of Luteolin and Erlotinib on LDH Release and Colony Assay

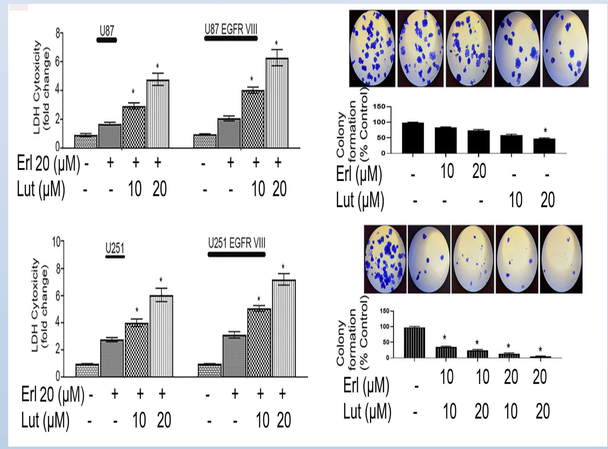


Figure 4.1A Effect of Luteolin and Erlotinib on Molecular Signaling Proteins

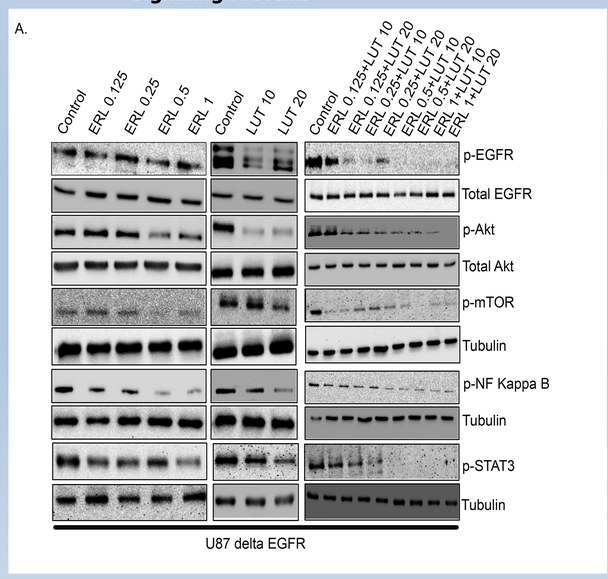
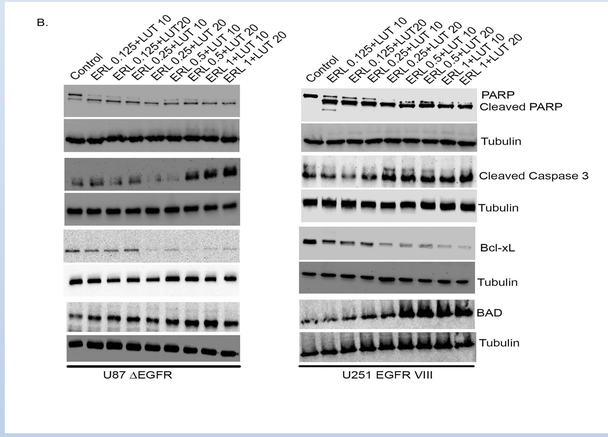


Figure 4.2. Effect of Gedunin on Molecular Signaling Proteins



Conclusion

- Results revealed that luteolin (10-20 μM) synergizes with erlotinib to decrease glioma cell proliferation.
- Luteolin and erlotinib attenuated signaling of downstream targets such as Akt/mTOR and NF kappa B
- Luteolin and erlotinib induced both PARP and caspase cleavages and decreased the expression of Bcl-xL, an antiapoptotic protein.
- **In conclusion, luteolin potentiated erlotinib-mediated decrease in cell proliferation and induced apoptosis in glioma cell lines by attenuating key survival signaling pathways and could serve as therapeutic molecules in the management of gliomas.**

References

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