Lophira alata induces a decrease in glioblastoma invasive growth in vitro

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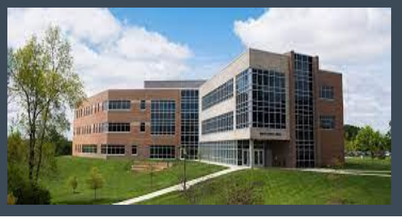


INTRODUCTION

- Malignant primary brain tumors cause more than 15,000 deaths per year[1]
- Five-year survival is approximately 36%[1]
- 50% of these tumors are GBM grade IV[1]
- Current treatment regimens against glioblastoma include radiotherapy with temozolomide and bevacizumab as adjunct therapies[2]. However, even with these multimodal therapeutic interventions, patients with glioblastoma have a very low prognosis and a 5-year survival rate of 36% due to its invasive and refractory nature of the tumor
- One of the signaling pathways that contribute to the aggressive behavior of glioma cells is the protein kinase C (PKC) pathway[3]
- Natural Products serves as sources of new drugs[4]
- The root of the plant *Lophira alata* (Ochnaceae) has been used as a component of traditional herbal decoctions administered to cancer patients in Africa[5]

OBJECTIVE

This study aimed to examined the cytotoxic potential of the methanolic fraction of *Lophira alata* root on malignant glioblastoma invasive cellular growth and survival.

METHODS

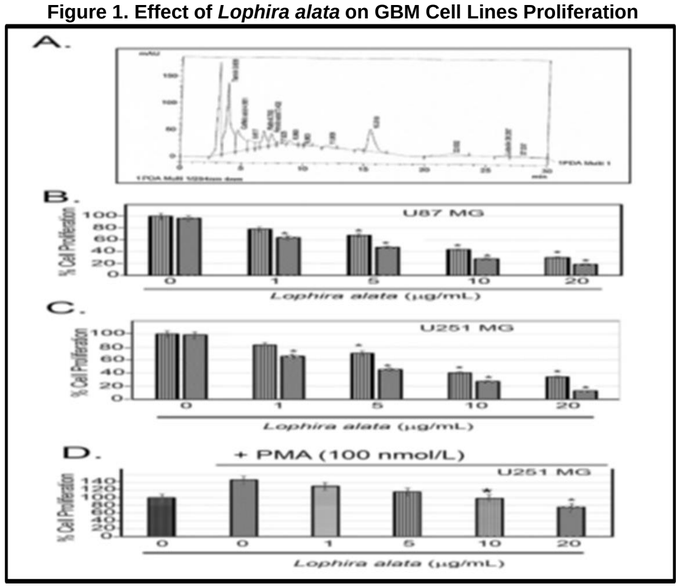
- Cell Lines: U87 and U251 MG cell lines
- Cell proliferation Studies---MTT Assay[6]
- Measurement and detection of LDH[7]
- Western Blot Analysis-cellular and apoptotic signaling[7]
- Caspase Assay[6]
- SiRNA Knockdown of PKC –alpha[6,8]

Statistical Analysis

Data are presented as the mean ± standard error. Differences between the groups were tested using by 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. Effect of *Lophira alata* on GBM Cell Lines Proliferation



RESULTS

Figure 2. Effect of *Lophira alata* on key molecular signaling targets in GBM Cell Lines

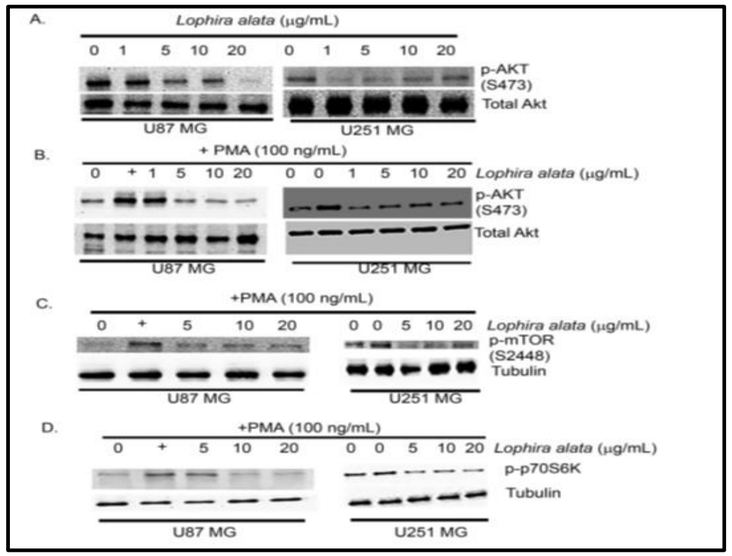


Figure 3. Effect of *Lophira alata* modulates PKC-alpha in GBM Cell Lines

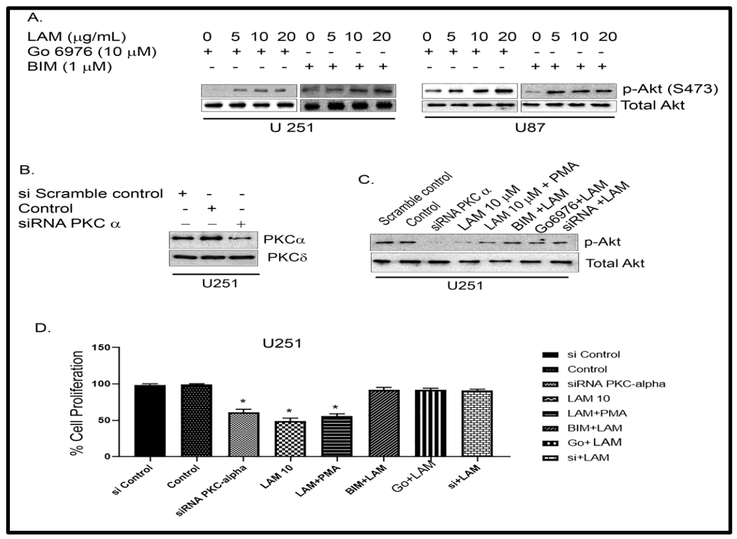
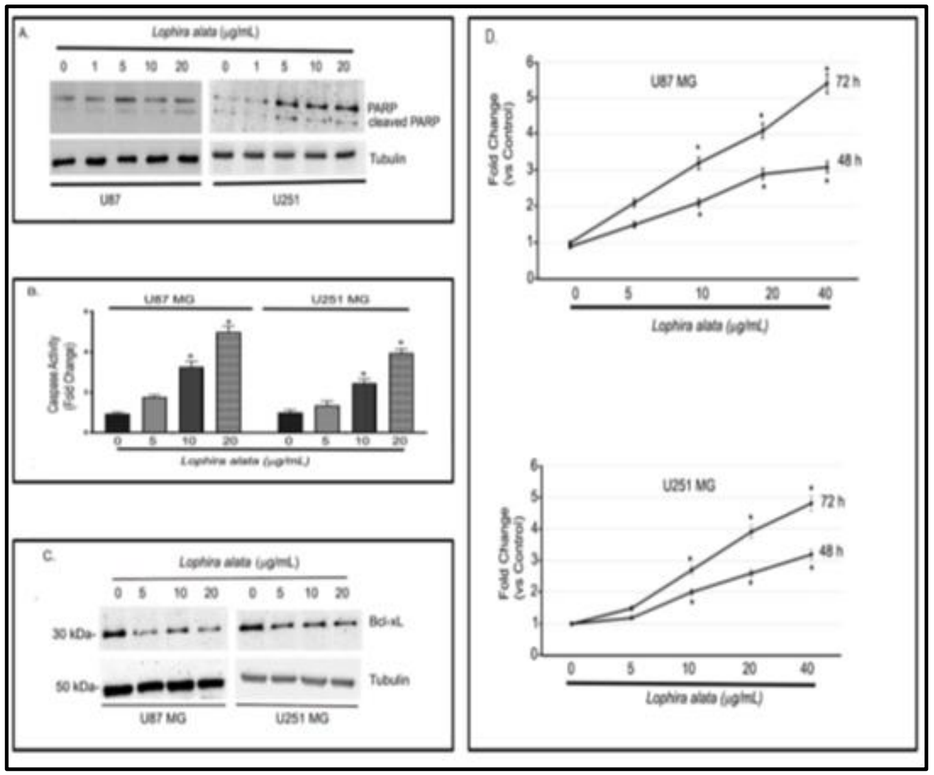


Figure 4. Effects *Lophira alata* on cellular apoptosis markers



CONCLUSIONS

Key findings

- This study found that the methanolic fraction of *Lophira alata* induced a concertation-dependent and time-dependent decrease in glioma cell proliferation.
- *Lophira alata* attenuated phorbol ester-mediated signaling of downstream targets such as Akt/mTOR.
- *Lophira alata* induced both PARP and caspase cleavages
- siRNA targeting PKC-alpha attenuated Lophira alata-mediated downregulation of Akt.

Conclusion

- ***Lophira alata* decreases cell proliferation and induces apoptosis in glioma cell lines and thus could serve as a therapeutic molecule in the management of gliomas.**

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