

**Studies on Antiproliferative and Proapoptotic Efficacy
of *Etlingera linguiformis* and *Smilax ovalifolia* using
Preclinical Lung Cancer Model.**

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*Summary and
Conclusion*

CHAPTER 5: SUMMARY AND CONCLUSION

Lung cancer is one of the top causes of mortality from cancer in India and throughout the globe. Although there are a number of well-known treatments, including as radiation, chemotherapy, and surgical removal, etc but their efficacy is limited with major consequences. Despite its widespread use, this treatment has a number of undesirable and often unpleasant side effects. While various phytochemicals have been identified and investigated for their antioxidant and subsequent anticancer effects, further elaborate research is considered necessary. However, the development of a reliable and reasonably priced anticancer medication remains a formidable obstacle. For this reason, it is crucial to look for pre-clinical studies that highlight the importance of preventing lung cancer and developing new, effective treatment strategies that are also less expensive, have fewer negative side effects, capable of oral administration and more precisely target cancer cells along multiple biological pathways associated with the disease. Traditional indigenous medical practices often include the use of plants due to their high potential for treating a wide range of illnesses, cancer included. Examples include ethnobotanical significant plants that are also widely used by locals but have not yet been studied for their potential anticancer therapeutic properties. However, as indicated by an ever-increasing number of research articles published throughout the globe, interest in plants with ethnomedicinal properties against many illnesses, including cancer, has exploded in recent years. The objective of the present studies is to learn more about the anticancer properties of ethnomedicinal plants *Etilingera linguiformis* (CAN) from the Zingiberaceae family and *Smilax ovalifolia* (LEX) from the Smilacaceae family, selected based on traditional knowledge of native people of Northeastern India. The findings of the present study reveals highly intriguing discoveries that may be utilized for in-depth study and perhaps be used to medication development. Presented below are the results of the current investigation.

- i). We have discovered that the CAN free phenolic fraction, the CAN bound phenolic fraction, the LEX free fraction, and the LEX bound phenolic fraction were all non-toxic to human PBMCs and Balb/C mouse model while preferentially killing the lung cancer cells (A549, NCI-H522, NCI-H23) and inhibited tumor growth in athymic nude mice model.
- ii). The phenolic fractions inhibited the cell viability up to less than 10% also induces cell death in dose dependent manner. The microscopic study elucidates the changes in

morphology of the lung cancer cells after exposed to phenolic fractions. The exposure of cancer cells to the phenolic fraction resulted in induction of apoptosis and autophagy.

- iii). We also observed increase in intracellular ROS levels, cellular modifications such as increased production of acid vesicles and accumulation of lipids in cancer cells but there was reduction in MMP level which correlates this apoptotic and autophagic pathway. It is quite possible that an imbalance in the homeostatic condition of the cancer cells would have resulted cell death.
- iv). In addition, we have found that the phenolic extract inhibited cell proliferation 29% to 72% with respect to the control.
- v). The exposed cancer cells were arrested in S phase 74% to 82%, G2/M phase 28% to 31% and apoptotic cells increased to 7% to 14% as compared to control. We have observed similar pattern of cell cycle arrest in Cisplatin treated A549 cells. The distribution of cells in S phase and G2/M phase 22% to 45% and 12% to 47% respectively.
- vi). The phenolic extract also inhibited the clonogenicity up to 5% to 35% and cell migration activity 8% to 20% compared to the respective control.
- vii). The pilot study on athymic nude mice has shown the antitumor activity of phenolic fraction.
- viii). The composite mixture of known anticancer phytochemicals along with some unknown molecular peaks present in the fraction that efficacy may have acted over lung cancer.

Our finding shows that the phenolic compound present in leaf extract of *Etingera linguiformis* and *Smilax ovalifolia* has very high potential to be explored for anticancer efficacy against lung cancer. The data generated in the present study may be validated in suitable in vivo lung cancer model for further confirmation. The finding may lead to novel anticancer agent which might have therapeutic implications. This might also find its potential in combinatorial therapy in effective management of lung cancer.