The Effects of Vitamin B1 analog, Benfotiamine, on the prevention of Non-Small Cell Lung Cancer

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Background

- Lung cancer is the most common in smokers and one of the leading causes of cancer related deaths.
- Current treatments for lung cancer include chemotherapeutic treatments, surgery, and FDA approved drugs that target certain cancer receptors.
- Side effects from these treatments varies per patient but nonetheless includes fatigue, nausea, hair loss, in conjunction to various other symptoms.
- Benfotiamine is a vitamin B1 analogue that has anti-oxidative and anti-inflammatory properties. However, its anti-carcinogenic potential is not clear.
- Therefore, we plan to examine how treatment of benfotiamine prevents non-small cell lung cancer cells growth in vitro and in vivo.

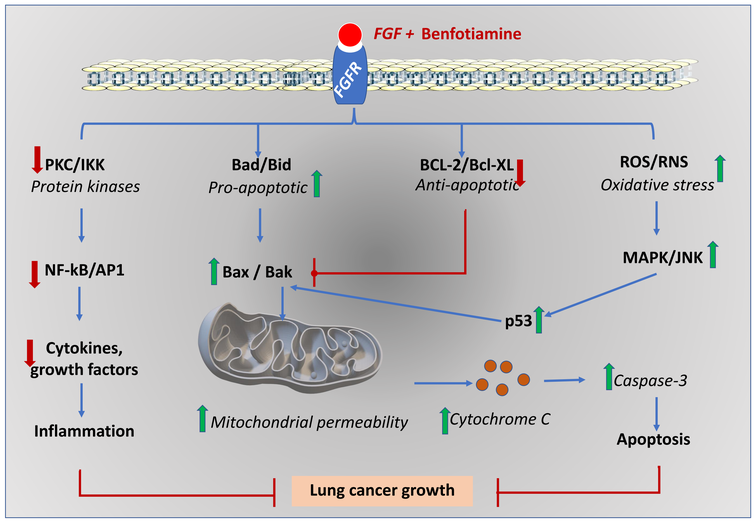

Figure 1: Benfotiamine prevents growth factor induced lung cancer cell growth by promoting the pro-apoptotic pathways and demoting the anti-apoptotic and anti-inflammatory pathways.

Hypothesis

We hypothesize that benfotiamine prevents lung cancer growth by regulating ROS/PKC/MAPK/NF-κB pathway and promoting the pro-apoptotic pathways.

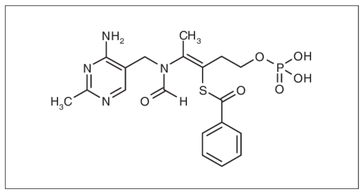

Figure 2. The chemical structure of benfotiamine

Vitamin B1 Could Prevent Lung Carcinogenesis

Proposed Methods

In vitro

- A549 non-small cell lung cancer cells will be treated with EGF (10 ug) ± Benfotiamine (0-100 uM) for 24 and 48 h.
- The cell growth and death will be determined by MTT and Annexin-V staining.
- Pro-and anti-apoptotic marker expression will be measured by specific array system.
- Activation of protein kinases will be measured by immunological methods.
- Activation of transcription factors will be determined by specific kits.
- Migration and invasion will be examined in the presence of benfotiamine.

In vivo

- Athymic nude mice will be injected with 1.5 million A549 cells sub-cutaneously on the dorsal side.
- When the tumor reaches a volume of 36-40 mm^3, the animals will be fed with diet containing benfotiamine (25 mg/kg).
- Tumor growth will be measured regularly, and when the tumor reaches around 2 cm in the controls, the animals will be euthanized, and tumors will be excised.
- Tumor volume will be recorded, tumor sections will be cut and immunohistochemical analysis for various carcinogenic markers will be determined.

Preliminary Results

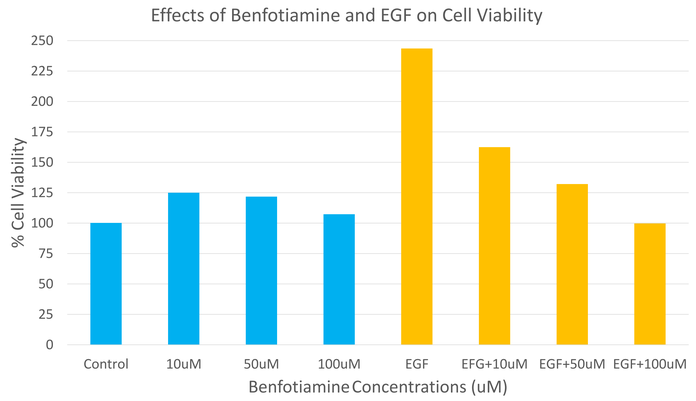

Figure 3: In the samples not treated with EGF we see minor changes to cell viability regardless of benfotiamine concentrations (blue). When treated with EGF and benfotiamine we see a decrease in cell viability with increasing concentration of benfotiamine (yellow).

Preliminary Results (Cont.)

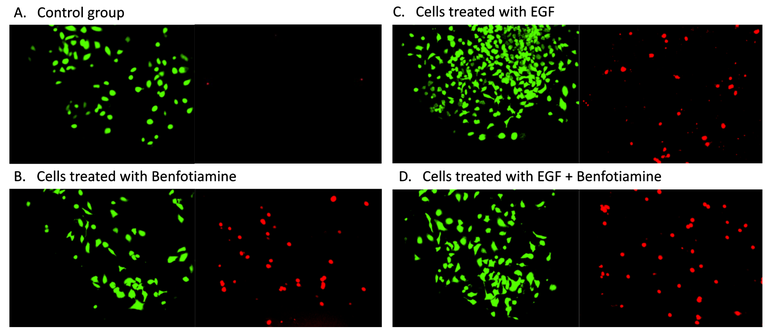

Figure 4: Photographs showing live (green) and dead (red) cells with the treatment of benfotiamine (B), EGF (C), and Benfotiamine + EGF(D), as well as our untreated cells (A).

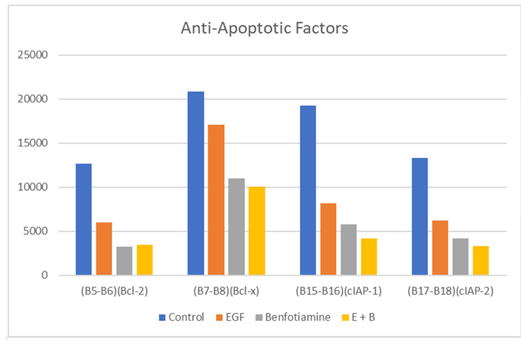

Figure 5: Our apoptosis protein array showed a decrease in anti-apoptosis factors, such as BCL-2, BCL-x, cIAP-1, cIAP-2.

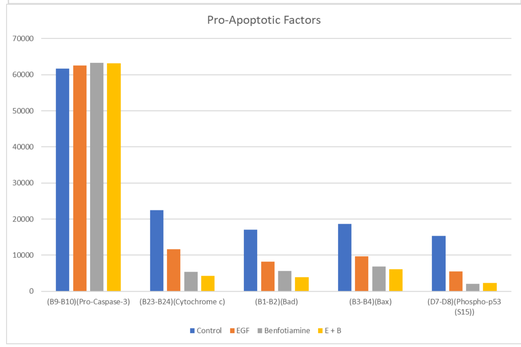

Figure 6: Our apoptosis protein array shows a decrease in pro-apoptosis factors (Caspase 3, Cytochrome C, BAD, BAX, p53), contrary to our original hypothesis.

For our *in vivo* study:

- We expect to see a decrease in tumor growth in the group that was supplemented with benfotiamine compared to the group that was not.

Conclusion

We hope to confirm our hypothesis that benfotiamine will reduce the growth of non-small cell lung cancer tumors specifically by promoting the pro-apoptotic pathways and demoting the anti-apoptotic and pro-inflammatory pathways.

*** Equal contribution**

NOORDA COLLEGE of OSTEOPATHIC MEDICINE