



Prevention of melanoma growth and invasion by lipophilic vitamin B1 derivatives.



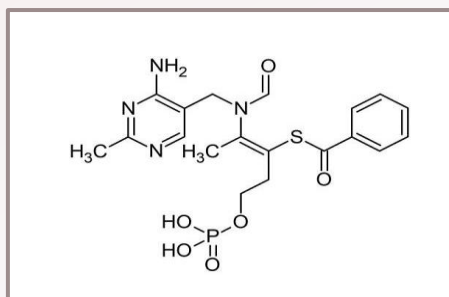
Sarah Ngo*, Nicholas Bleza*, Alexandria Vo & Kota V Ramana
Department of Biomedical Sciences, Noorda College of Osteopathic Medicine, Provo, UT

Background

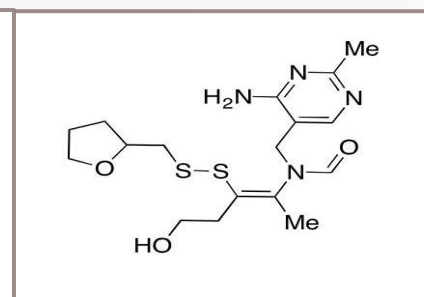
In the United States, melanoma is one of the most common cancers among Americans. According to the Skin Cancer Foundation, 1 in 5 Americans will develop melanoma by the age of 70. Having even 5 or more sunburns can double the risk for melanoma. In fact, research has shown that increased oxidative stress due to unprotected exposure to UV light and tanning beds leads to damage to skin cells and melanoma progression. Currently, surgical removal of the cancer cells is the initial treatment for melanoma. Surgical excision, however, does not eliminate the risk of developing new melanocytic neoplasms in the future. Increased free radicals generated by oxidative stress could lead to genomic instability and mutations that trigger the development and growth of melanoma. Vitamins, including vitamin B1, are molecules readily used by biological systems to counteract oxidative stress and have been shown to modulate inflammatory response. Thus, the usage of vitamins as a preventative therapy for at-risk patients is a promising approach to decreasing the incidence and progression of melanoma. Currently, there is insufficient research on the chemopreventive efficacy of Vitamin B1 derivatives, Benfotiamine and Fursultiamine.

Purpose

To investigate the anti-carcinogenic potential of water-soluble thiamine derivatives, Benfotiamine and Fursultiamine, in melanoma progression and metastasis. We propose to use B16-F10 cells, melanoma cells from C57BL/6 mice, and mouse model of melanoma to understand the molecular mechanisms through which thiamine derivatives prevent melanoma.



Benfotiamine



Fursultiamine

Hypothesis

We hypothesized that the potential anti-oxidative and anti-inflammatory actions of thiamine derivatives are beneficial for preventing melanoma cell growth and invasion.

Methods

- Murine melanoma cells, B16-F10, were obtained from American Type Culture Collection (ATCC) and maintained with Dulbecco's Modified Eagle's Medium (DMEM) media.
- Cells were treated and incubated with varying concentrations of Benfotiamine and Fursultiamine for 24 hours.
- 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) Assay to detect the Cell Viability and Proliferation: Utilizes cellular metabolic activity measurements as an indicator of cell viability, proliferation, and cytotoxicity.
- RD systems Mouse Apoptosis Arrays to detect the cell expression of Pro- and Anti-Apoptotic markers with Vitamin B1-derivatives: This multiplex antibody-based array determines various anti- and pro-apoptotic, survival and inflammatory markers involved in cell growth and death from a single sample.

The following tests are pending:

- Scratch assay and Trans-well cell migration assay to detect Invasion and Migration of the melanoma cells: Measures their chemotactic capability towards a chemo-attractant and extracellular matrix invasion of the melanoma cells which is a crucial process to cancer metastasis.
- Caspase-3 Assay Kit to assess apoptosis and mechanism of apoptosis: Measures Caspase-3 activity in biological samples.
- Mouse model of melanoma: In-vivo study of melanoma on mice to measure effectiveness of vitamin B1 treatment.

Results

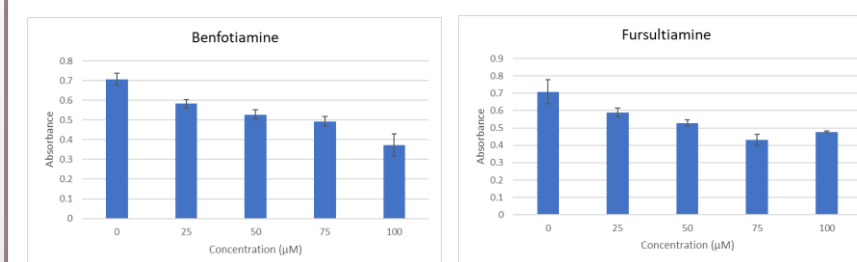


Fig 1: Vitamin B1 derivatives prevent melanoma cells growth.

Results

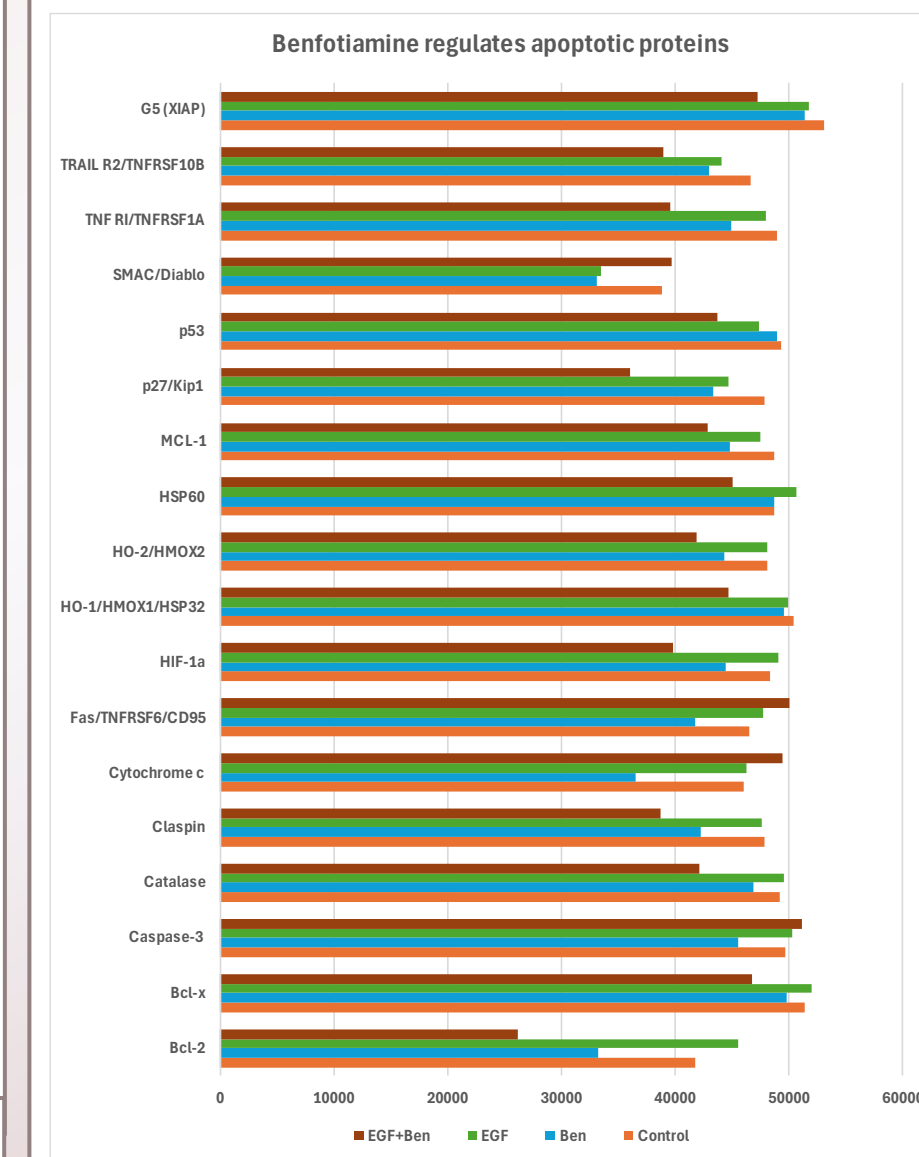


Fig. 2: Regulation of anti-, and pro-apoptotic proteins by Benfotiamine.

Conclusion

Our preliminary results suggest that lipophilic vitamin B1 derivatives effectively prevent melanoma cell growth indicating their chemo-preventive effects in B16-F10 cells. Further experiments are currently undergoing in the lab to confirm apoptotic properties.

