

Alteration of Prostate PC3 Cell Eicosanoid Metabolism by Zyflamend[®], a Unique Multi-Herbal Preparation with Potent Anti-inflammatory Activity

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INTRODUCTION

Zyflamend[®] consists of standardized concentrated extracts from plant products (ginger, rosemary, tumeric root, holy basil, green tea, hu zhang, Chinese goldthread, barberry, oregano, and Baikal skullcap) typically consumed in an Eastern diet. The relationship between inflammation and diseases such as cancer is now well established but determining which components of inflammation are critical for etiology and exacerbation of specific diseases remains a challenge. For example, while our data has shown that Zyflamend can potently potent cyclooxygenase enzymes (cloned COX-1 and COX-2 activities), the ability to reduce growth of human prostate tumor cell growth produced by this product is believed to be in large part due to COX-2 independent mechanisms (D. Bemis, Ph.D., Columbia Univ., personnel communication). This study represents initial experiments aimed at elucidating the effects of Zyflamend on inflammation pathways and the role that this product may have in prevention and/or treatment of malignant disease.

METHODOLOGY

Using a novel LC/MS/MS based method that simultaneously determines multiple prostaglandins, lipoxygenase products, leukotrienes and related bioactive lipids involved in inflammation, we examined changes in eicosanoid metabolism in cells and tissues produced by this unique herbal product. Western blot analyses were used to determine changes in enzyme protein concentrations.

RESULTS

Endogenous levels of intracellular PGE₂, 12-HETE as well as 5-HETE declined in a concentration-dependent manner upon exposure of human prostate PC3 cells to Zyflamend®. In contrast, cellular levels of 15-HETE and 13-HODE, typically considered to be beneficial in controlling aberrant cell growth, were elevated. The elevation of 13-HODE was dramatic but, surprisingly, was due to a high content of 13-HODE present in Zyflamend itself and was not dependent on cellular generation of this important eicosanoid. The 13-HODE levels were determined to be high enough to account for inhibition of tumor cell growth that was independently verified by addition of authentic 13-HODE to tumor cell cultures. Exposure of human tumor cells (PC3 prostate) to Zyflamend also resulted in the down regulation of 5-LOX expression as determined by Western blot analyses. The ability of Zyflamend to block arachidonic acid mediated mouse ear inflammation was also assessed. This product produced significant inhibition of LTB₄ synthesis and up-regulated the production of 15-HETE. A detailed analysis of the role of Zyflamend in inhibiting activation of the transcription factor NF-κB will also be presented.

CONCLUSIONS

Zyflamend is a potent concentrated multi-herb product that suppresses cell and tissue inflammation through COX and LOX mediated pathways. In addition, it is a potent inhibitor of NF-κB activation suggesting that downstream inhibition of genes associated with inflammation and malignant cell growth are also inhibited. The use of concentrated multi-herb products, such as Zyflamend may provide a novel and effective means of inflammation control and disease prevention. [Supported by a grant from New Chapter, Brattleboro, VT].

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