THE IMPACT OF ANTIOXIDANTS ON THE CYTOTOXIC PROPERTIES OF CAPSAICIN

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Introduction

Capsaicin has exerted potent anti-cancer properties by enouncing anti-proliferative, apoptotic and anti-metastatic activity. To the best of our knowledge, the specific cell targets and successive mechanism of cytotoxic activity of capsaicin in different type of malignant cells, still remains unclear and contradictory.
The aim of this study is to examine the influence of a combination of a few common antioxidants, which possess particularly high antioxidative potential, as a reason to inhibit the cytotoxic activity of pure capsaicin. This is due to the synergistic antioxidative effect of capsaicin and other co-extracted bioactive compounds (vitamin C, vitamin E and some flavonoids).

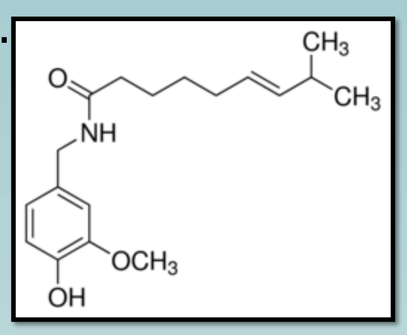

Fig.1 Molecular structure of capsaicin

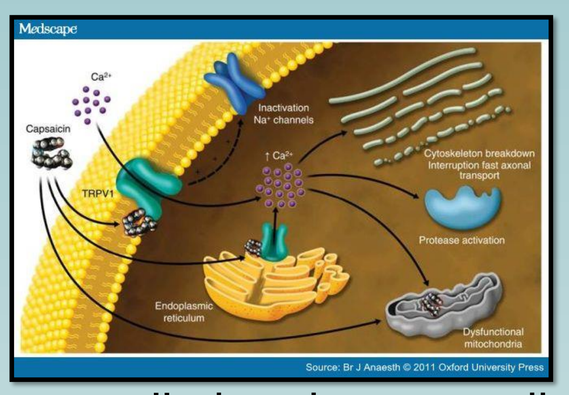

Fig.3 Binding of capsaicin to TRPV1 receptor

The ability of capsaicin to inhibit the growth of different cancer cells is primary mediated by its ability to induce apoptosis. It has been reported that two different pathways are mainly mediating the process of activation of apoptosis.

Intrinsic pathway is the most common pathway of capsaicin induced apoptosis

The mechanism of intrinsic pathway of apoptosis is distinguished by intracellular activation of apoptosis through intracellular stressors, in which the most common are reactive oxygen species (ROS) and excess intracellular calcium. Disruption of the mitochondrial membrane and alterations in bcl-2, Bax, bcl-xL, and bad proteins, can cause a release of cytochrome C in cell cytosol and subsequent activation of the caspase cascade. These processes are the initial triggers that are eventually leading to apoptosis (Zhang et al., 2008). Cytochrom C together with some other factors can induce activation of caspase-9. Activated capsasa-9 can lead to activation of caspasa 3 and 7, which cleaves the inhibitor of caspasa activated DNAase and results in DNA fragmentation. Many studies examining the cytotoxic effects of capsaicin on prostate and other malignant cell lines, have reported that capsaicin induced apoptosis is linked to intrinsic mechanisms, related to the increase in ROS.

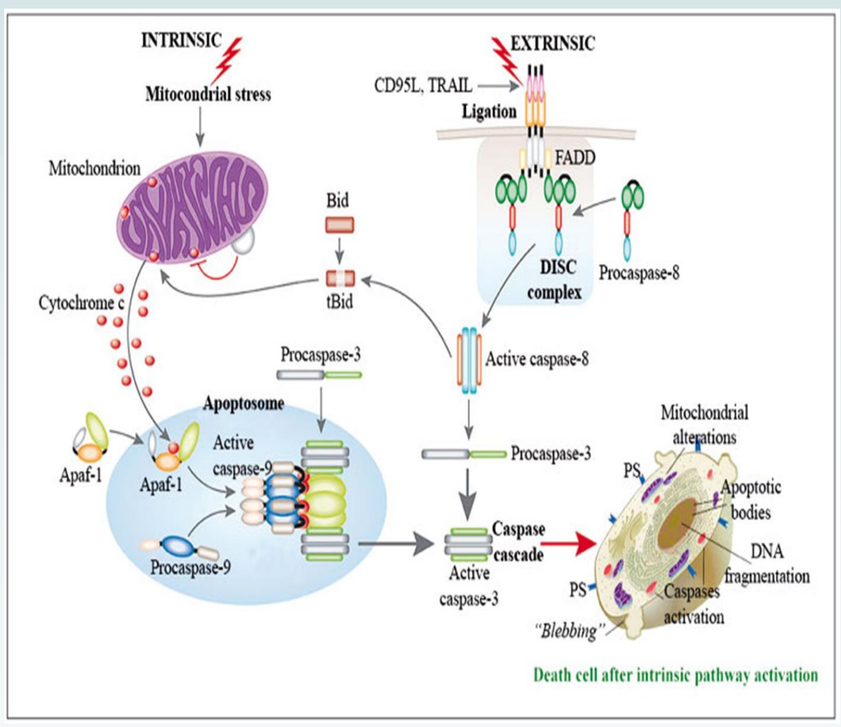

Fig.3 Intrinsic and extrinsic apoptosis pathways

Our previous results

In a previous study, we have shown that *Capsicum* extracts did not showed cytotoxic activity on neuroblastoma cells, beside the cytotoxic properties of capsaicin, itself, at concentrations 0.5 mmol/L to 2.1 mmol/L. As shown in the literature, one of the mechanisms of capsaicin cytotoxicity that has been proposed support the production of reactive oxygen species on cellular level. This leads to disruption of mitochondrial membrane potential, activation of caspase-3 activity and successive apoptosis. We assumed that this phenomenon of synergism on the antioxidative effect between capsaicin and other bioactive compounds present in the extracts could be a possible reason for inhibition of the cytotoxic effect of capsaicin.

Conclusion: This data should stress out the importance of a balanced intake of antioxidants while using a cytotoxic agent, which acts as a prooxidnat in cancer cells.

References

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