

A Novel Mixture Containing Ascorbic Acid, Lysine, Proline, and Green Tea Extracts Inhibits Critical Parameters in Angiogenesis

M.W. Roomi, V. Ivanov, T. Kalinovsky, A. Niedzwiecki, M. Rath

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In this book chapter, we have presented the results of our studies proving the efficacy of a micronutrient synergy approach in cancer through multiple mechanisms. As such, in addition to blocking the secretion of matrix metalloproteinase enzymes (MMPs) and consequently connective tissue degradation, the synergistic micronutrient mixture could also inhibit several factors involved in the formation of new blood vessels (angiogenesis) – an essential process supporting the growth of tumors.

In the *in vivo* studies, we observed that the mice receiving the micronutrients in their diet developed 53% smaller tumors with less blood supply than the mice fed a control diet.

We investigated the effects of micronutrients on secretion of the main angiogenesis promoting factors, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), angiopoietin-2, platelet derived growth factor (PDGF) and tumor growth factor (TGF). We observed a significant reduction in the expression of all these factors. The main angiogenic factors- VEGF and FGF - were decreased by 72% and 45%, respectively.

Our *in vitro* studies confirmed significant reduction in angiogenesis by the micronutrient combination through different mechanisms, including decreased attachment and migration of endothelial cells required for the formation of microtubules and then new blood vessels. Additionally, we also observed that the micronutrient mixture was able to disrupt the already formed smaller blood vessels as well. These results indicate that the micronutrients not only reduce the new tubule formation, they also help in destruction of already formed blood vessels thereby starving the cancer cells.

The special staining also revealed that the secretion of enzymes, MMP-2 and MMP-9, was completely blocked indicating decreased destruction of the surrounding connective tissue, thereby arresting growth and metastatic potential of the tumor.