10th Brazilian Conference on Natural Products
XXXVI RESEM
4-7 November 2025, Belo Horizonte, MG, Brazil

Section: 03

CYTOTOXIC EFFECT OF CAROTENOIDS ON GASTRIC CANCER CELLS VIA A POTENTIAL PRO-OXIDANT MECHANISM

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Carotenoids are dietary compounds widely recognized for their antioxidant properties. However, under specific conditions, they may act as pro-oxidants, increasing intracellular reactive oxygen species (ROS) and triggering cytotoxic effects. This dual behavior has sparked growing interest in their potential application in cancer treatment. Nonetheless, the relationship between their pro-oxidant potential and cytotoxicity in gastric cancer remains unclear. This study aims to evaluate the cytotoxic effect of food-relevant carotenoids on a gastric adenocarcinoma cell line (AGS) through a three-phase approach.

In the first phase, cytotoxicity was assessed using the MTT assay in AGS and human keratinocytes (HaCaT) treated with five dietary carotenoids: β-carotene, astaxanthin, lutein, zeaxanthin, and fucoxanthin. Fucoxanthin and β-carotene showed the most promising results, with IC_{50} values of 13.92 ± 2.97 µM and 60.35 ± 1.84 µM in AGS cells, respectively, and markedly lower IC_{50} in HaCaT cells. This suggests differential sensitivity between tumor and non-tumor models. AGS and HaCaT were selected due to their relevance as gastric cancer and non-tumor epithelial models in toxicological and pharmacological screening.

The second phase focused on intracellular ROS quantification using the H_2DCFDA fluorescent probe. Contrary to expectations, a reduction in ROS levels was observed in AGS cells under all treatments. However, this may reflect the loss of viable, metabolically active cells rather than a true antioxidant effect. Since the ROS signal was not normalized to live cell count, current efforts aim to normalize fluorescence values to viability data to better interpret these results. Each treatment was tested at multiple concentrations and timepoints to evaluate both immediate and delayed oxidative responses.

The third phase, in progress, will apply NMR-based metabolomics to elucidate metabolic disruptions induced by the most active carotenoid. These findings may guide future research and support the rational use of dietary carotenoids as potential adjuvants in gastric cancer therapy.

Keywords: *Carotenoids; Gastric cancer; Pro-oxidant activity; Reactive oxygen species (ROS).*