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LETTER TO THE EDITOR – **post-print version**

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Nutraceuticals as potential therapeutic agents for preventing gastric cancer: towards targeting chronic inflammation

Nutracéuticos como potenciales agentes terapéuticos para prevenir el cáncer gástrico: rol de la inflamación crónica

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Dear editor:

Gastric cancer (GC) has been consistently ranked among the top malignancies affecting humans after lung, breast, colon/rectum, prostate and skin cancers. It represents the world's fifth-most frequent malignancy and the third leading cause of cancer death¹. This type of cancer arises from malignant cells in the stomach lining and can thus be categorized into two topographic subsites: cardia gastric cancers, which arise closest to the esophagus, and non-cardia cancers, which arise in the distal portions of the stomach¹. Chronic inflammation caused by *Helicobacter pylori* infection and autoimmune gastritis complicates the development of these two major types of gastric cancer, though adenocarcinomas, which arise from epithelial cells in the chronically inflamed gastric mucosa, account for more than 90% of stomach cancers². Even though *Helicobacter pylori* has been identified as a carcinogen and a major cause of GC, many gastric illnesses have been implicated in the disease, including chronic gastritis, stomach and duodenum ulcers, and lymphomas of the mucosa-associated lymphoid tissue system³. Gastric cancer is caused by several risk factors, including infections, diet, genetics, lifestyle, and the environment, all of which can be avoided by making adjustments to avoid the risk factors.

Chronic inflammation is a term used to describe the inflammatory response marked by continuing immune cell recruitment and tissue damage as a result of the persistent inflammatory responses. Inflammation represents an old evolutionary process that involves the activation, recruitment, and action of innate and adaptive immune cells as well as tissue repair, regeneration, remodeling, and tissue homeostasis management⁴. While pro-inflammatory cytokines such as IL8, TNF, IL10, IL1B, and IL1RN are implicated in higher risk of gastric cancer², others such as IL35, IL27, IL23, and IL12 are elevated in gastric cancer cell lines and tissue from *H. pylori*-infected subjects⁵. Cytokines such as IL33, IL32, and IL10 have also been identified to be expressed in the inflamed stomach mucosa and elevated level of IL-1 and IL-6 have been linked to non-scirrhus type gastric cancer, human gastric carcinoma growth and progression⁶ (Fig.1). Among nutraceuticals targeting inflammatory cytokines include allicin, the active ingredient in fresh crushed garlic, which lowered the expression of IL-8 and IL-1beta levels and inhibited secretion of IL-1beta, IL-8, IP-10, and MIG from the two cell lines in a dose-dependent manner⁷. Apigenin, kaempferol and resveratrol also exert inhibitory effects on the TNF-alpha⁸, whereas the capsaicin derived from green and red pepper also inhibited the interleukin-6-induced STAT3 activation⁹. Flavonoids such as morin, rutin, quercetin, Fisetin, Luteolin, Naringenin were reviewed to have modulatory effects on cytokines and inflammatory pathways¹⁰.

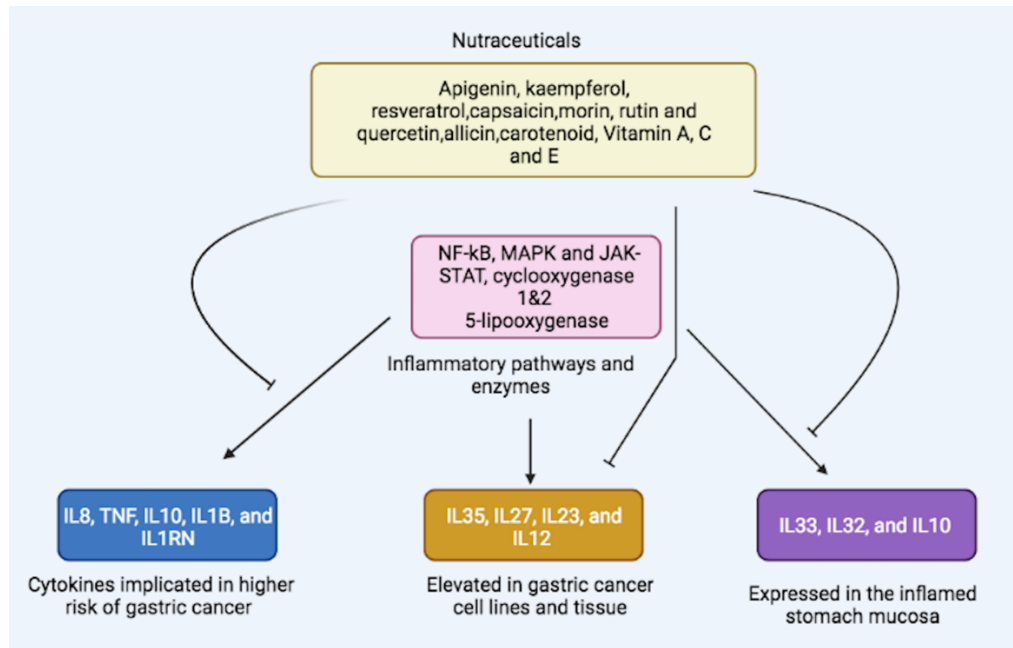


Figure 1. Nutraceuticals modulating cytokines implicated in gastric cancer via pathways and enzymes

Nutraceuticals encompasses pharmaceutical alternatives possessing physiological benefits including vitamins, amino acids, minerals, and other dietary ingredients, extracts, or derivatives that have potential health advantages beyond their nutritive benefits. Several foods, nutrients, and non-nutrient food components appear to play a role in chronic inflammation management. These substances can target inflammatory mediators while also reducing macromolecular oxidation. Vitamin E, for example has been demonstrated to have antitumor, anti-metastasis and chemo preventive effects in gastric cancer¹¹, presumably by suppression of the NF-κB pathway, inhibition of HMG-CoA reductase, DNA polymerases, and specific protein tyrosine kinases and protein kinase C¹². Low dosages of vitamins, particularly vitamin A, vitamin C, and vitamin E, can considerably reduce the incidence of GC¹³. Several phytochemicals such as resveratrol, quercetin, curcumin, and anthocyanins, may inhibit inflammation via suppressing prostaglandin production and the NF-κB pathway via enhancing/inhibiting cytokine production as the case may be¹⁴. In order to reduce the current trends on gastric cancer, it is recommended that we should keep away from the various risk factors, abstain from alcohol, tobacco usage, smoked and pickled meals, as well as salted meats and fish. Therefore, we should consume a lot of fresh fruits and vegetables as well as whole grains including whole grain pasta, bread, cereal, and rice. One approach is to use experimentally proven supplements containing nutraceuticals to reduce our risk of developing this malignancy.

COMPETING INTERESTS

The author declares no conflict of interest.

AUTHOR'S CONTRIBUTION

The sole author, ISZ is responsible for the content, figure, and conclusion of this letter

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