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### LETTER TO THE EDITOR

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

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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 death<sup>1</sup>. 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 stomach<sup>1</sup>. 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 cancers<sup>2</sup>. 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 system<sup>3</sup>. 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

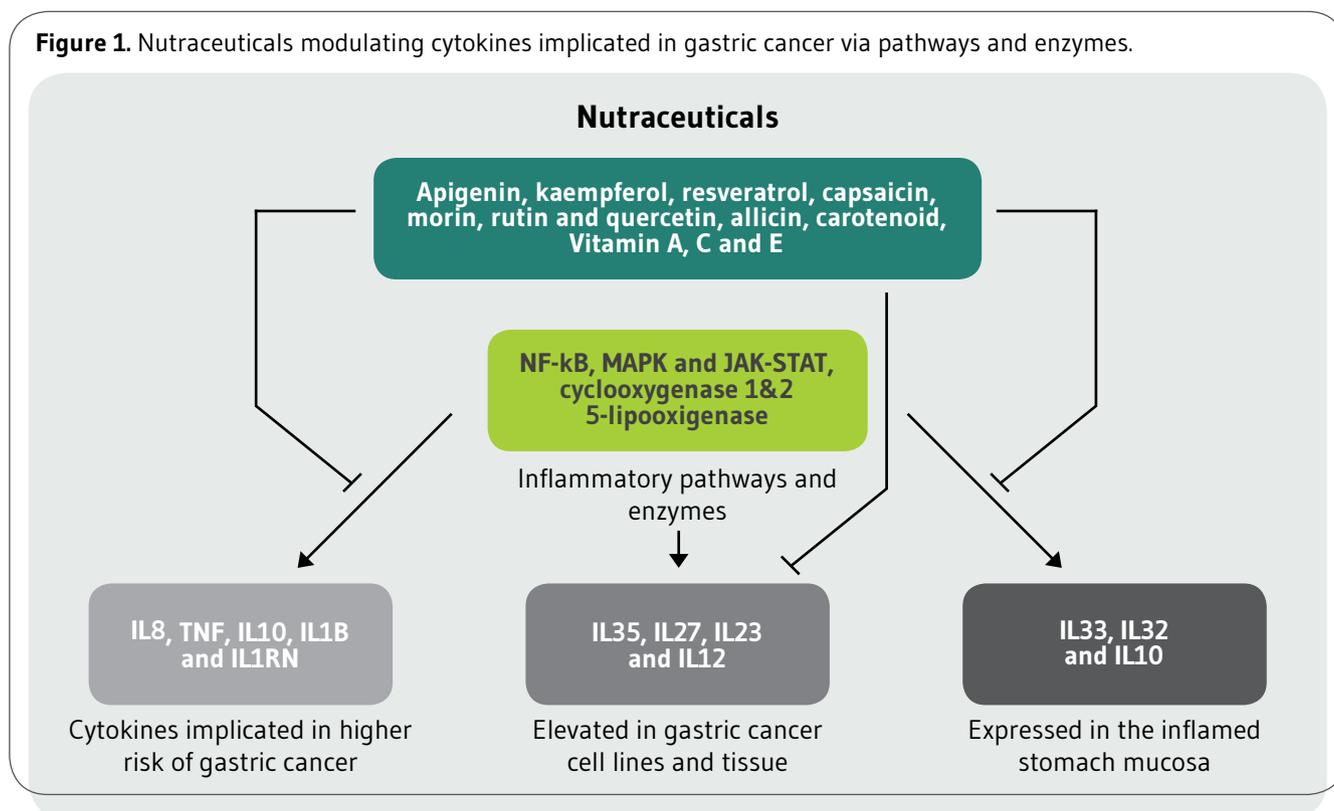


recruitment and tissue damage as a result of the persistent inflammatory responses. Inflammation represents an old evolutionary process that involves the activation, recruitment, and action of innate and adaptive immune cells as well as tissue repair, regeneration, remodeling, and tissue homeostasis management<sup>4</sup>. While pro-inflammatory cytokines such as IL8, TNF, IL10, IL1B, and IL1RN are implicated in higher risk of gastric cancer<sup>2</sup>, others such as IL35, IL27, IL23, and IL12 are elevated in gastric cancer cell lines and tissue from *H. pylori*-infected subjects<sup>5</sup>. 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-scurrhous type gastric cancer, human gastric carcinoma growth and progression<sup>6</sup> (Figure 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 manner<sup>7</sup>. Apigenin, kaempferol and resveratrol also exert inhibitory effects on the TNF-alpha<sup>8</sup>, whereas the capsaicin derived from green and red pepper also inhibited the interleukin-6-induced STAT3 activation<sup>9</sup>. Flavonoids such as morin, rutin, quercetin, Fisetin, Luteolin, Naringenin

were reviewed to have modulatory effects on cytokines and inflammatory pathways<sup>10</sup>.

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 cancer<sup>11</sup>, presumably by suppression of the NF-kB pathway, inhibition of HMG-CoA reductase, DNA polymerases, and specific protein tyrosine kinases and protein kinase C<sup>12</sup>. Low dosages of vitamins, particularly vitamin A, vitamin C, and vitamin E, can considerably reduce the incidence of GC<sup>13</sup>. Several phytochemicals such as resveratrol, quercetin, curcumin, and anthocyanins, may inhibit inflammation via suppressing prostaglandin production and the NF-kB pathway via enhancing/inhibiting cytokine production as the case may be<sup>14</sup>. In order to reduce the current trends on gastric cancer, it is recommended that

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



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.

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### REFERENCES

- (1) Agudo A, Cayssials V, Bonet C, Tjønneland A, Overvad K, Boutron-Ruault M-C, et al. Inflammatory potential of the diet and risk of gastric cancer in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Am J Clin Nutr.* 2018; 107(4): 607-16. doi: 10.1093/ajcn/nqy002.
- (2) Bockerstett KA, DiPaolo RJ. Regulation of Gastric Carcinogenesis by Inflammatory Cytokines. *Cell Mol Gastroenterol Hepatol.* 2017; 4(1): 47-53. doi: 10.1016/j.jcmgh.2017.03.005.
- (3) Ekström AM, Held M, Hansson LE, Engstrand L, Nyrén O. Helicobacter pylori in gastric cancer established by CagA immunoblot as a marker of past infection. *Gastroenterology.* 2001; 121(4): 784-91. doi: 10.1053/gast.2001.27999.
- (4) Greten FR, Grivnickov SI. Inflammation and Cancer: Triggers, Mechanisms, and Consequences. *Immunity.* 2019; 51(1): 27-41. doi: 10.1016/j.immuni.2019.06.025.
- (5) Al-Sammak F, Kalinski T, Weinert S, Link A, Wex T, Malferteiner P. Gastric epithelial expression of IL-12 cytokine family in Helicobacter pylori infection in human: is it head or tail of the coin? *PLoS One.* 2013; 8(9): e75192. doi: 10.1371/journal.pone.0075192.
- (6) Kai H, Kitadai Y, Kodama M, Cho S, Kuroda T, Ito M, et al. Involvement of proinflammatory cytokines IL-1beta and IL-6 in progression of human gastric carcinoma. *Anticancer Res.* 2005; 25(2A): 709-13.
- (7) Lang A, Lahav M, Sakhnini E, Barshack I, Fidler HH, Avidan B, et al. Allicin inhibits spontaneous and TNF-alpha induced secretion of proinflammatory cytokines and chemokines from intestinal epithelial cells. *Clin Nutr.* 2004; 23(5): 1199-208. doi: 10.1016/j.clnu.2004.03.011.
- (8) Kowalski J, Samojedny A, Paul M, Pietsz G, Wilczok T. Effect of apigenin, kaempferol and resveratrol on the expression of interleukin-1beta and tumor necrosis factor-alpha genes in J774.2 macrophages. *Pharmacol Rep.* 2005; 57(3): 390-4.
- (9) Bhutani M, Pathak AK, Nair AS, Kunnumakkara AB, Guha S, Sethi G, et al. Capsaicin is a novel blocker of constitutive and interleukin-6-inducible STAT3 activation. *Clin Cancer Res.* 2007; 13(10): 3024-32. doi: 10.1158/1078-0432.CCR-06-2575.
- (10) Leyva-López N, Gutierrez-Grijalva EP, Ambriz-Perez DL, Heredia JB. Flavonoids as Cytokine Modulators: A Possible Therapy for Inflammation-Related Diseases. *Int J Mol Sci.* 2016; 17(6): E921. doi: 10.3390/ijms17060921.
- (11) Liu H-K, Wang Q, Li Y, Sun W-G, Liu J-R, Yang Y-M, et al. Inhibitory effects of gamma-tocotrienol on invasion and metastasis of human gastric adenocarcinoma SGC-7901 cells. *J Nutr Biochem.* 2010; 21(3): 206-13. doi: 10.1016/j.jnutbio.2008.11.004.
- (12) Aggarwal BB, Sundaram C, Prasad S, Kannappan R. Tocotrienols, the vitamin E of the 21st century: its potential against cancer and other chronic diseases. *Biochem Pharmacol.* 2010; 80(11): 1613-31. doi: 10.1016/j.bcp.2010.07.043.
- (13) Kong P, Cai Q, Geng Q, Wang J, Lan Y, Zhan Y, et al. Vitamin intake reduce the risk of gastric cancer: meta-analysis and systematic review of randomized and observational studies. *PLoS One.* 2014; 9(12): e116060. doi: 10.1371/journal.pone.0116060.
- (14) Prakash D, Kumar N Cost Effective Natural Antioxidants. En: Gerald JK, Watson RR, Preedy VR, editores. *Nutrients, Dietary Supplements, and Nutraceuticals: Cost Analysis Versus Clinical Benefits.* Totowa, NJ: Humana Press; 2011. p. 163-87.