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File: ■ Turmeric (*Curcuma longa*)
■ Green Tea (*Camellia sinensis*)
■ Curcumin
■ Epigallocatechin-3-Gallate
■ Non-Hodgkin's Lymphoma

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RE: Curcumin and EGCG Induce Remission in B-cell Non-Hodgkin's Lymphoma Patients

Bassiouny AR, Atteya MA, El-Rashidy FH, Neenaa HM. Curcumin and EGCG suppress apurinic/apyrimidinic endonuclease 1 and induce complete remission in B-cell non-Hodgkin's lymphoma patients. *Functional Foods in Health and Disease*. 2011;1(12):525-544.

According to the authors, the incidence of non-Hodgkin's lymphoma (NHL) is increasing, making it the fifth most common cancer in Egypt. Elevated levels of apurinic/apyrimidinic endonuclease/redox factor-1 (APE1) in cancers are indicators of poor prognosis and chemotherapeutic resistance, and the removal of APE1 sensitizes cancer cell lines to chemotherapeutic agents.[1] The efficacy of chemotherapy is increased with the multitargeted regulation of multiple signaling pathways, including nuclear factor-kappa B (NF-κB), cyclooxygenase-2, apoptosis, and others. These authors hypothesized that curcumin, a polyphenolic antioxidant derived from turmeric (*Curcuma longa*), and epigallocatechin-3-gallate (EGCG) from green tea (*Camellia sinensis*) would increase the efficacy of chemotherapy in patients with follicular lymphoma (FL), a type of NHL. They evaluated the antitumor effect of curcumin and EGCG in combination with chemotherapy on peripheral blood mononuclear cells in patients with lymphoma.

Curcumin and EGCG were selected because they are pharmacologically safe agents that have been shown to down-regulate NF-κB and NF-κB-regulated gene products involved in tumor angiogenesis and metastasis.

The authors recruited 40 subjects: 10 healthy subjects (control group) and 30 subjects diagnosed with FL (FL group). The 18 men and 12 women that made up the FL group were diagnosed with FL at different stages, with histological subtypes.

Blood samples were drawn from all subjects at baseline, and at 3, 6, 9, and 12 months. Physical activity and the extent of disease were assessed at baseline.

During the study period, the subjects in the FL group were treated for 9 months with either the chemotherapy regimen CHOP, CHOP with curcumin, or CHOP with curcumin and EGCG (CHOP includes cyclophosphamide, hydroxydaunorubicin [also called doxorubicin or Adriamycin], oncovin [vincristine], and prednisone or prednisolone). Subjects were followed for 3 months subsequent to the 9-month treatment.

The herbal treatment capsules were compatible with curcumin doses between 0.9 and 5.4 g daily (Curcuminoids C^3 Complex®; America's Finest, Inc.; East Windsor, New Jersey) and 9 g of green tea whole extract daily (1,000 mg tablets of green tea extract containing 200 mg EGCG; Techno-med; Egypt).

CHOP resistance was defined as occurring in subjects whose disease progressed during first-line CHOP chemotherapy or who relapsed within 6 months after treatment. Drug resistance is a major cause of relapse and the incurability of cancer. The effect of the herbal therapy to overcome the drug resistance of FL subjects to chemotherapy was estimated by determining glutathione s-transferase (GST) activities. GST helps defend against free radicals, peroxides, xenobiotics, and carcinogens.

Attainment of complete remission was the most important predictor of overall survival; low serum lactate dehydrogenase (LDH), limited stage disease, and a high serum albumin were also independently associated with prolonged survival.

The authors report that adding curcumin and EGCG to the CHOP treatment significantly lowered cytoplasmic APE1, and the levels of the transcription factor were lower than those predicted from the effects of the CHOP agents alone. Eighteen of the subjects had a complete remission, and 12 patients had partial remission within the 9-month treatment period and the 12-month follow-up period. They remained disease-free for a mean of 8.6 years (range=7.9-9.2 years) after the combination therapy. According to the authors, this report provides the first data demonstrating a role of APE1 in lymphoma patients' survival and function after CHOP treatment.

In those subjects treated with a combination of CHOP, curcumin, and EGCG, the serum levels of the angiogenic vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) were significantly higher than those of the control subjects before treatment. Significantly reduced serum levels of both factors were reported in all subjects receiving the combination of CHOP, curcumin, and EGCG as a first response of the treatment. No P values were given.

Further results indicate that adding curcumin to CHOP improved the International Prognostic Indices (β2 microglobulin and LDH activity) and caused a significant decrease in both groups of combination therapy after 6 and 9 months of treatment, while with green tea, the effect was greater than that of curcumin alone. The chemotherapy-treated group did not show any significant difference in both factors. The decrease in these parameters was a good prediction for complete remission rate and a good prognostic effect of both curcumin and green tea, say the authors.

GST activity showed a marked increase in the CHOP-only group after 9 months of treatment and at the 3 month follow-up, while in both combination therapy groups, GST activity showed a significant decrease. "This gives us an idea about the ability of both adjuvant therapies (curcumin and EGCG) to overcome the resistance of NHL patients to chemotherapy," write the authors.

Evaluation of hepatic and renal function during treatment indicated the absence of any adverse side effects of the studied adjuvant therapy (curcumin and green tea) in combination with chemotherapy.

Treatment of patients' cells with the combination of CHOP, curcumin, and EGCG for 9 months induced significant cell death versus the control, CHOP, or CHOP and curcumin-treated cells. The number of viable cells reduced significantly ($P<0.05$).

The authors conclude that in the subjects with FL, the combination of curcumin and EGCG resulted in a synergistic antitumor activity and, with CHOP agents, down-regulated the expression of all NF-κB-regulated gene products, leading to the suppression of angiogenesis, metastasis, and entering in complete remission as indicated by β2 microglobulin and LDH levels. The addition of curcumin and EGCG to CHOP achieved long-lasting remissions in 18 of 30 (60%) subjects with FL. "These data suggest that the combination of curcumin, EGCG, and CHOP is [a] highly effective palliative regimen for patients with FL with good performance status," write the authors.

—Shari Henson

Reference

[1]Fishel ML, He Y, Reed AM, et al. Knockdown of the DNA repair and redox signaling protein Ape1/Ref-1 blocks ovarian cancer cell and tumor growth. *DNA Repair (Amst)*. 2008;7(2):177-186.

Referenced article can be found at http://www.functionalfoodscenter.net/files/49449692.pdf.