P.O. Box 144345 Austin, TX 78714-4345 ▪ 512.926.4900 ▪ Fax: 512.926.2345 ▪ www.herbalgram.org

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FILE: ▪Tea (*Camellia sinensis*)
▪Skin Toxicity
▪Inflammation

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RE: Tea Extracts Effective for Reducing Skin Inflammation Due to Radiation Therapy

Pajonk F, Riedisser A, Henke M, McBride WH, Fiebich B. The effects of tea extracts on proinflammatory signaling. *BMC Med.* December 1, 2006;4(28):1-12.

Skin toxicity is a common side effect of radiation therapy in people with cancer. Skin toxicity causes discomfort and reduces quality of life during and after radiation therapy. When severe, skin toxicity can lead to interruptions in radiation therapy, which may reduce the effectiveness of cancer treatment. Skin toxicity that is rated as grade 2 or higher is usually caused by inflammation in the irradiated area. Tea (*Camellia sinensis*) contains polyphenol compounds with anti-inflammatory activity, and various tea extracts have been studied to see if tea can protect against skin damage caused by radiation. The purpose of this study was to determine the effects of topically-applied tea extracts on the duration of radiation-induced skin toxicity and to investigate the underlying mechanisms for the effects of tea extracts.

The study was conducted at the University Hospital of Freiburg in Freiburg, Germany. The study included a retrospective review of data from previously treated cancer patients and laboratory tests of the effects of tea extracts on human and animal cells. In the retrospective review, data from 60 cancer patients who experienced skin toxicity of grade 2 or higher during radiation therapy were evaluated. The review included 31 patients with head and neck cancers, 25 patients with pelvic region cancers (primarily anal carcinoma), and 4 patients with other cancers. All patients received standard skin care during radiation therapy, consisting of daily treatment with moisturizing cream, until a condition known as moist desquamation occurred. From that point until the moist desquamation disappeared, preparations of green tea or black tea were applied to the affected skin for 10 minutes, three times a day. The condition of the skin was evaluated daily by the medical staff.

Several in vitro tests were conducted using white blood cells from healthy humans and macrophage cells from mice. Macrophages are immune cells that destroy bacteria and foreign particles and that produce immune-regulating chemicals known as cytokines. In the first test, human cells were incubated with green or black tea extracts (made by steeping black tea bags in boiling water and green tea bags in 70°C water for 5 minutes) and levels of cytokines were measured before and after exposure to lipopolysaccharide (LPS). LPS is a bacterial toxin that stimulates production of inflammatory cytokines in human cells. In the second test, proteasome activity of macrophage cells

was measured. Proteasomes are large protein complexes that break down unneeded proteins and enzymes. In the third test, extracts of black tea or green tea or the tea polyphenol epigallocatechin gallate (EGCG) were added to the macrophage culture and the cell culture was exposed to radiation. Cell proliferation was measured after 5 days of growth.

The retrospective review of cancer patients treated with topical tea extracts compared the impact of black tea extract and green tea extract on the duration of grade 2 or higher skin toxicity. For patients with head and neck cancers, the mean duration of toxicity was similar for black tea extract (17 ± 1.8 days) and green tea extract (16.5 ± 1.7 days). For patients with pelvic region cancers, the mean duration of toxicity was significantly ($P < 0.014$) shorter for green tea extract (16.3 ± 1.6 days) than black tea extract (22.2 ± 2.1 days). Previous studies report mean skin toxicity durations of 26 days for patients with head and neck cancers and 22 days for patients with anal carcinoma.

In the first in vitro test, both black tea and green tea extracts decreased the secretion of inflammatory cytokines in human cells stimulated by LPS. The effect of the tea extracts was dose dependent, with higher levels of tea extract yielding greater inhibition of inflammatory cytokine secretion, and the inhibition was greater with green tea extracts than black tea extracts. In the second in vitro test, both green tea and black tea extracts inhibited proteasome activity and blocked proinflammatory cell signaling. Black tea extracts inhibited proteasome activity more effectively than green tea extracts. In the third in vitro test, moderate concentrations of green tea extract, black tea extract, and EGCG slightly protected mouse macrophage cells from radiation damage.

According to the authors, this study demonstrates that topically-applied tea extracts help to restore skin integrity in people with radiation-induced skin toxicity. The in vitro models used in this study demonstrate that tea extracts inhibit the release of proinflammatory cytokines, influence proteasome activity, and slightly protect macrophages from radiation damage. Based on the differences in cell responses to green tea extract, black tea extract, and EGCG, the authors conclude that tea extracts involve multiple, complex pathways, some of which are dependent on compounds other than anti-inflammatory polyphenols. They suggest that tea extracts offer an inexpensive and widely available treatment for radiation-induced skin damage.

This study emphasizes the importance of evaluating the effects of whole plant extracts in addition to isolated plant constituents known to have biological effects. The article could be strengthened by providing information on the absorption of tea compounds by the skin and discussing the potential for application of antioxidant-containing substances to interfere with the effectiveness of radiation therapy. In the future, controlled clinical trials should be conducted to directly compare the effects of topical tea extracts with standard care or placebo treatment in patients undergoing radiation therapy.

—Heather S. Oliff, PhD

Enclosure: Referenced article is an Open Access article through BioMed Central.