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File: ■ Polyphenols
■ Common Cold
■ Immune System

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RE: Combined Green Tea, Grape, and Shiitake Mushroom Extracts for Treating Common Cold Symptoms Found Beneficial

Schütz K, Saß M, de With A, Graubaum HJ, Grünwald J. Immune-modulating efficacy of a polyphenol-rich beverage on symptoms associated with the common cold: a double-blind, randomized, placebo-controlled, multi-centric clinical study. *Br J Nutr*. May 21, 2010:1-9. [epub ahead of print]. doi:10.1017/S0007114510002047

Polyphenolic compounds from green tea (*Camellia sinensis*) and grapes (*Vitis vinifera*) possess immune-stimulating effects. Polysaccharides from shiitake mushrooms (*Lentinula edodes*), particularly β-glucans, have also demonstrated immunomodulatory effects. In this randomized, placebo-controlled, clinical trial, researchers have tested the effect of a standardized polyphenol-rich beverage containing extracts of green tea, grape seed, grape skin, and shiitake mushrooms (extraction medium unspecified), plus vitamin C, in the treatment of the common cold.

The multicenter, prospective, clinical trial was conducted by researchers from the University Hospital Charite, Humboldt University in Berlin, Germany between February and August 2004. The researchers recruited patients through advertisements, from the practices of the clinical investigators, and through local pharmacies. They enrolled 100 patients aged 20-65 years. Eligible patients scored at least 5 out of 15 points on a scale that measures the severity of 5 common cold symptoms: headache and/or joint pain, sore throat and/or difficulty swallowing, hoarseness and/or cough, and nasal congestion. Each symptom was rated from 0 (not present) to 3 (strong). The patients were randomized to receive a placebo or the study beverage using EDGAR (Experimental Design Generator and Randomiser).

For 10 days, the patients took 250 ml of their assigned beverage twice daily. Clinical investigators examined the patients at baseline, after 3-6 days of treatment, and after 7-10 days of treatment. Physicians assessed the severity of the 5 cold symptoms. The primary efficacy measure was the change in physician-rated symptoms. The physicians also scored the severity of local findings on a scale of 0 (not present) to 2 (strong), including “reddening of the Waldeyer’s ring or tonsils,” “granulation and/or myxorrhoea on the pharyngeal wall,” and herpes labialis. The researchers assessed safety through

clinical data, laboratory safety measures, global evaluations by clinicians and patients, and adverse events. The patients rated the severity of 5 cold symptoms (general feeling of sickness, headache and/or joint pain, throat problems, hoarseness and/or cough, and nasal congestion/sniffle) twice daily in patient diaries.

The placebo beverage was a red soft drink containing sugar, water, citric acid, and flavoring. It had a similar appearance and flavor to the polyphenol beverage under investigation. The polyphenol beverage was standardized to contain 1,400 mg/L polyphenols measured with the Folin-Ciocalteu method and expressed as gallic acid equivalents (GAEs). It contained 3 g/L green tea extract, 12 g/L grape peel extract, 0.5 g/L grape seed extract, 0.05 g/L shiitake mushroom extract, and 0.3 g/L vitamin C. The investigators measured the antioxidant capacities of both beverages using the following methods: Trolox-equivalent antioxidant capacity (TEAC), ferric-reducing ability of plasma (FRAP), and photochemical luminescence. They also measured the levels of individual polyphenols and total polyphenols.

Out of 100 patients, 2 patients (1 from each group) were excluded due to the loss of their case report forms, and 2 patients from the placebo group ended the study early. Of these 2 withdrawals, 1 patient who attended the second study visit and not the final visit was included, and 1 patient who did not attend the second study visit was excluded. In the placebo group, 1 patient failed to return the patient diary, but was included in the final analysis. This left 49 patients in the treatment group and 48 in the placebo group. The authors did not observe significant changes in the safety parameters or the clinical data in either group, except for reduced body temperature in the polyphenol group ($P=0.003$). The group's average body temperature remained in the normal range. In the placebo group, 1 patient reported "sour burps" and nausea during the first 3 days of the study. There were no other adverse event reports. The patients and clinical investigators rated the tolerability as "very good" for the polyphenol beverage and "good" for the placebo drink. The placebo beverage provided 91 mg/L total phenols, while the polyphenol beverage contained 1,437 mg/L total phenols. The polyphenol beverage contained 77.7 mg/L gallic acid, 35.6 mg/L catechin, 127.2 mg/L epigallocatechin gallate (EGCG), 54.5 mg/L epicatechin, and 28.5 mg/L epicatechin gallate. In addition, the polyphenol drink had greater antioxidant activity compared to the placebo beverage.

At baseline, the average total symptom score was 10 in both groups. By the second visit, the average total symptom scores had dropped by 3.6 points in the treatment group and by 1.3 points in the placebo group, resulting in a significantly lower score in the treatment group ($P<0.001$). Between the second and third study visits, the total symptom scores had dropped a further 8.1 points in the treatment group and 4.2 points in the placebo group. After 3-4 days of the treatment, the patients' diaries showed significantly improved cold symptoms in the polyphenol group compared to the placebo group ($P<0.01$), except for "the general feeling of sickness" which was not significantly different until the fifth day ($P<0.01$). All patients in both groups "showed reddening of the Waldeyer's ring and/or the tonsils" at baseline, but this parameter was much lower in the treatment group compared to the placebo group at the end of the study ($P<0.05$). The majority of patients in both groups were experiencing granulation and myxorrhoea on the back of the throat at baseline, but at the end of the study, there were significantly more patients with these symptoms in the placebo group than in the treatment group ($P<0.01$). At the end of the study, significantly fewer patients in the polyphenol group had herpes labialis compared to the placebo group ($P<0.05$).

At the third study examination, 38.8% of treatment group patients and 8.3% of placebo group patients were complaint-free (P<0.001). The patients' diaries indicated that 41.9% of the treatment group and 5.0% of the placebo group patients had no cold symptoms on the evening of the seventh study day (P<0.001). On the third day of treatment, the treatment group experienced a significant improvement in sleep reduction compared to the placebo group (P<0.01). By the fourth day, the treatment group experienced a significant improvement in the disturbance of daily activities compared to the placebo group (P<0.01). On day 7, the treatment group was using half as many tissues as the placebo group (P<0.01). The use of additional cold treatments was not significantly different between the groups. In the treatment group, the majority of physician global efficacy ratings were "good" (42.9%) or "very good" (34.7%), and the majority of patient global efficacy ratings were "very good" (42.9%) or "good" (30.6%). In contrast, the physician global efficacy ratings for the placebo group were primarily "moderate" (42.6%) or "bad" (31.9%), and the majority of patient global efficacy ratings were "bad" (40.4%) or "moderate" (34.0%).

The authors conclude, "The present study clearly indicates that patients suffering from common cold symptoms benefit from the consumption of the investigated polyphenol-rich and shiitake extract-containing beverage." The broad spectrum improvement in symptoms has led the authors to conclude that the observed effects were due to a general improvement in immune function, which could be attributed to green tea and grape polyphenols. Further research is needed to determine if the shiitake extract and vitamin C also contributed to the observed immunomodulatory effects. Additional studies are needed to confirm these results.

—Marissa Oppel-Sutter, MS

The American Botanical Council has chosen not to reprint the original article.