

Olive and Whey Products May Soothe Psoriasis

BY ERIK L. GOLDMAN
Contributing Writer

Two new natural products—one containing olive polyphenols and the other a proprietary combination of whey proteins—can reduce the symptom burden and appearance of mild to moderate psoriasis.

Both products were recently introduced in the United States as oral formulations, filling a void left by drug therapy development for psoriasis over the last decade, which has largely involved oral medications for severe disease. The cost and side-effect profiles for the various biologics make them largely inappropriate for mild disease.

Polyphenols extracted from olives are potent antioxidants. Several years ago, Japanese researchers found that polyphenols can also down-regulate inflammation and improve psoriatic plaques.

In the grand tradition of serendipitous medical discoveries, Dr. Fujio Numano, a cardiologist at the Tokyo Vascular Disease Institute, observed the antipsoriatic effect while studying the cardiovascular effects of a proprietary olive polyphenol formula called Olivenol. This compound, which comes from water pressed out of organic olives, contains high levels of hydroxytyrosol, a very strong antioxidant.

Dr. Numano, who died in 2005, was one of Japan's leading cardiovascular researchers. Toward the end of his career he became interested in the role of oxidative stress and inflammation in heart disease. Several years before his death, Dr. Numano became aware of Olivenol, which is produced by CreAgri, a Hayward, Calif., nutraceutical company. He decided to test it in the context of heart disease.

He enrolled 35 heart disease patients in an open-label trial of Olivenol, with the object of assessing its impact on patients' lipid profiles, inflammatory markers, and overall cardiovascular health. It turned out that 8 of the 35 had skin disorders, including several with psoriasis. Dr. Numano noticed that most of these patients experienced significant improvement in their skin conditions while taking the olive polyphenols.

Roberto Crea, Ph.D., a biochemist who first identified the antioxidant potential of hydroxytyrosol as well as a practical method for extracting it from the water byproduct of olive oil production, recalled in an interview: "Dr. Numano contacted me and said he had a big surprise. He told me one of his patients, a 71-year-old with widespread psoriasis who was on heavy immunosuppressive drugs, showed remarkable improvements after several months on the Olivenol. After 2 months, 80% of the lesions had disappeared."

Cautious about jumping to premature conclusions, Dr. Numano recruited several other people with psoriasis or inflammatory skin disorders like allergic contact dermatitis, erythema nodosum, and seborrheic dermatitis. The Olivenol formula gave measurable, sometimes marked improvement in all of the patients within 8 months, said Dr. Crea, who is chairman of the board and chief scientist for CreAgri.

He was not entirely surprised by the apparent anti-inflammatory effect since in vitro experiments with the polyphenol formula showed that it could inhibit tumor necrosis factor- α , interleukin-1, and lipoxigenase-5.

Dr. Numano's work is intriguing, but Dr. Crea stressed that it is far too soon to call Olivenol a true therapy for psoriasis. His

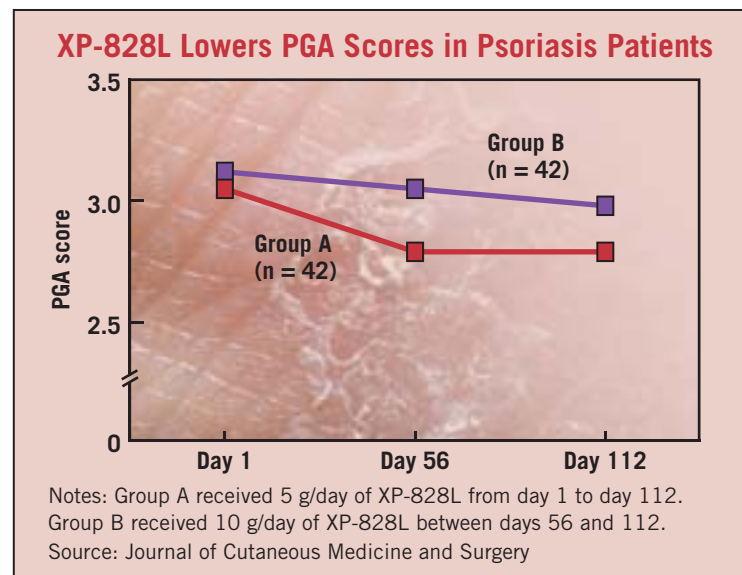
company is planning to fund a formal controlled clinical trial of Olivenol in psoriasis patients. The product is currently available as an antioxidant dietary supplement.

The second natural product, whey, a common byproduct of dairy food production, is proving to be a cornucopia of anti-inflammatory and immunomodulatory proteins, some of which appear to improve inflammatory diseases like psoriasis.

Dr. Yves Poulin and his colleagues at the Centre de Recherche Dermatologique du Québec Métropolitain have been studying a proprietary formulation of whey proteins, called XP-828L, in patients with mild to moderate disease. The formula was developed by Advitech, a Canadian company focused on developing evidence-based nutraceutical products. Dr. Poulin did not disclose any conflicts of interest, but one of his associates is vice president of research and development for Advitech.

The investigators randomized 84 patients with confirmed mild to moderate psoriasis (27 women, 57 men) to treatment with either a food grade cellulose placebo or 5 g/day of the whey protein powder. Patients were instructed to take the assigned treatment orally between their morning and evening meals. After 56 days, the placebo-treated patients were switched to 10 g/day of the whey proteins, while those who received treatment from the outset remained on the lower 5-g daily dose.

All patients discontinued all other antipsoriatic therapies at least 28 days prior to beginning the trial. They were assessed by blinded investigators at two different medical centers on day 56 (8 weeks) and day 112 (16 weeks). Investigators used Physician's Global Assessment (PGA) scores, Psoriasis Area and Severity Index



(PASI), body surface area measurement, and patient-rated itch severity in their assessments.

In the intent-to-treat analysis, patients receiving the XP-828L formula showed a statistically significant reduction in PGA scores from a mean of 3.05 at baseline to 2.79 after 8 weeks. There was no significant difference in the placebo-treated patients, whose scores went from 3.12 to 3.05. Exclusion of the 15 patients who did not complete the protocol did not change the finding in any way.

There was a trend toward greater improvement in the PASI scores among patients receiving the whey proteins, but the differences between the two groups were not significant (*J. Cutan. Med. Surg.* 2006;10:241-8).

There were no major differences on any of the assessment scales at 16 weeks, following the period in which placebo-treated patients were switched to the 10-g daily dose of the whey proteins. Their PGA scores improved more or less to the level seen in the patients treated with the lower dose, who generally maintained their improvements but did not obtain any additional benefit after the first 8 weeks.

The investigators concluded that "a period of 56 days of treatment with 5 g/day of XP-828L is sufficient to induce and maintain a clinical improvement of mild to moderate psoriasis." Though it is clearly no competition for the biologics or other advanced drug therapies, the whey protein formulation can reduce symptoms and severity in many cases.

Moreover, it can do so with minimal risk of adverse effects. There were no clinically apparent side effects from the whey proteins at either the 5-g or 10-g daily dose, and there were no changes in creatinine, total bilirubin, transaminase enzymes, or other biochemical markers.

The precise mechanisms underlying the whey protein effects are not entirely clear, but Dr. Poulin noted that whey contains beta-lactoglobulin, alpha-lactalbumin, lactoferrin, immunoglobulins, and growth factors that have immunomodulatory effects.

In vitro work shows that XP-828L can inhibit production of Th1 cell cytokines, especially IFN-gamma and IL-2, which would presumably have a down-regulatory effect on T-cell-mediated disorders like psoriasis. ■

Psoriasis Risk Increased by Smoking History, Passive Exposure

BY ROBERT FINN
San Francisco Bureau

Women who smoke cigarettes increase their risk of developing psoriasis by 78%, according to a large prospective, longitudinal study.

The increased risk appears to be dose dependent, wrote Dr. Arathi R. Setty of Harvard Medical School, Boston, and colleagues. The highest risk occurred among women with a history of at least 21 pack-years of smoking. Those women more than doubled their risk of developing psoriasis. Women with a history of 11-20 pack-years incurred a 60% increase in risk and those with a history of 1-10 pack-years

had a 20% increase in risk compared with women who never smoked. These results are all statistically significant and are all adjusted for age, body mass index, and alcohol intake (*Am. J. Med.* 2007;120:953-9).

The study involved 79,628 female registered nurses enrolled in the Nurses Health Study II (NHS II). The investigators excluded 1,096 women with a history of psoriasis at baseline. In 1991, when this study began, the average age of the women enrolled was 35.5 years and their average BMI was 24.5 kg/m².

At baseline, 66% of the women reported never having smoked, 23% reported being former smokers, and 11% reported being current smokers.

During 14 years of follow-up, the investigators documented 887 incident cases of psoriasis for an overall incidence of 1.1%. Fifty-six percent of the cases occurred among women who had never smoked.

The investigators found that current smokers who reported smoking at least 25 cigarettes per day were 2.5 times as likely to develop psoriasis as were those who never smoked. Past smokers who had smoked for at least 20 years were 57% more likely to develop psoriasis than were those who had never smoked.

Dr. Setty and associates also reported that women who quit smoking decreased their risk of developing psoriasis. Women who quit less than 10 years previously

had a 61% elevated risk compared with women who never smoked, those who quit 10-19 years previously had a 31% elevated risk, and those who quit 20 or more years previously showed no statistically significant increase in risk.

Exposure to passive smoke was an additional significant risk factor for developing psoriasis. Women whose mothers smoked while pregnant with them had a 21% increased risk, compared with women with no prenatal exposure. Women who were exposed to passive smoke as children had an 18% increase in risk, but women who were exposed as adults experienced no significant increase in the risk of developing psoriasis. ■