

# Oral Soy Supplementation and Dermatology

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Presently, using botanicals to enhance the appearance of skin, hair, and nails appears to be increasingly popular. The tremendous rise in direct sales of spa, boutique, and proprietary skin care lines and oral supplements makes a basic understanding of the ingredients in these products important for the dermatologist. Soy is probably the most notable of all botanicals, since it can be administered both topically and orally in a variety of forms for a variety of purposes. This article examines the use of soy to enhance the appearance of skin, hair, and nails.

Soybeans are a rich source of flavonoids, which form a large group of plant polyphenols that are divided into anthocyanins, flavones, flavonols, and isoflavones. The anthocyanins are responsible for the blue to red colors present in flowers and fruits. The flavones, flavonols, and isoflavones are colorless to yellow and are biologically active compounds that can function as antioxidants, as well as inhibit enzyme function through receptor binding. Most flavonoids in plants are found in the glycoside form, meaning that they are attached to a sugar molecule. This allows the chemical moiety to be water soluble and remain within the aqueous plant vacuoles. However, the glycosides are biologically inactive in humans, since they do not have the proper physical structure to bind to cellular receptors. These glycosides can be converted to the active form after oral administration, when the hydrolytic intestinal enzymes remove the sugar molecule, converting the flavonoids to the biologically active form.<sup>1</sup>

Soy flavonoids also undergo this chemical reaction when administered orally.<sup>2</sup> The flavonoid found in the highest concentration in soy is genistin, which is present in the glycoside's inactive form. The flavonoid can be converted to its aglycon form, the molecular form without the sugar, in the intestine, becoming the potent protein

kinase inhibitor genistein. Protein kinases are important cell-signaling pathways in the skin that can lead to the expression of enzymes that degrade collagen and elastin. Matrix metalloproteinases, activated by oxygen radicals and inflammatory cytokines, are an excellent example of these enzymes.<sup>3</sup> Genistein, found primarily in fermented soy products such as tofu and roasted soy nuts, can block these signaling pathways.

Several mouse studies have been published demonstrating the protective effect of genistein against photoaging and photocarcinogenesis. In hairless mice, both topical and oral administration of genistein inhibited the initiation and promotion of photocarcinogenesis, resulting in reduced tumor incidence and multiplicity.<sup>4</sup> The effects were greater with topical administration of genistein than with oral administration, and the reduction in photocarcinogenesis was dose related. Wei et al<sup>4</sup> also demonstrated that 5 mmol of genistein applied topically to both mouse and human skin reduced sunburn severity.

Genistein is structurally similar to estrogen and can bind to some of the same receptors. This is why genistein is considered a phytoestrogen and is credited with decreasing cardiovascular disease and breast cancer in Asian women.<sup>5</sup>

There are 2 estrogen receptors in the human body:  $\alpha$  and  $\beta$ . Genistein has lower affinity for the human  $\alpha$  receptor but the same affinity for the human  $\beta$  receptor as endogenous human estrogen.<sup>6</sup> Thus, it can exert end-organ effects when administered orally.

Genistein also demonstrates some skin effects that are unrelated to estrogen. For example, it inhibits tyrosine protein kinase and mitogen-activated protein kinase that modulate cell growth and differentiation.<sup>7</sup> It also interferes with lipid metabolism by inhibiting phosphodiesterase and increasing lipolysis. It may also inhibit the proliferation of preadipocytes.<sup>8</sup> For this reason, oral genistein has been recommended to treat cellulite, a condition with reduced incidence in cultures that consume large amounts of soy.

Soy isoflavones have also been studied for their benefit in alopecia areata in a mouse model. McElwee et al<sup>9</sup> demonstrated that dietary consumption of soy oil reduced the

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incidence of alopecia areata in a dose-response fashion. In this study, the incidence of alopecia areata in soy oil-treated mice was 86%, 39%, and 18% in mice receiving 1%, 5%, and 20% soy oil, respectively. The authors also reported that only 4 of 10 mice injected with genistein developed alopecia areata compared with 9 of 10 control mice. Thus, soy may modulate hair growth and the immune system.

Topical administration of soy provides a variety of benefits. Topical genistein has been reported to function as a potent antioxidant, scavenging peroxy radicals and protecting against lipid peroxidation *in vivo*.<sup>10</sup> This is the mechanism for its topical antiaging effects. However, soy also contains 2 proteinase inhibitors: the Kunitz trypsin inhibitor, also known as the soybean trypsin inhibitor, and the Bowman-Birk inhibitor.<sup>11</sup> These proteinase inhibitors are found only in fresh soy milk, not fermented soy products as with genistein. The Kunitz trypsin inhibitor reduces the proteolytic activity of trypsin for the formation of a stable stoichiometric complex. It consists of 181 amino acids with 2 disulfide bridges spherically shaped. The Bowman-Birk inhibitor is an 8-kd protein that inhibits both trypsin and chymotrypsin. Both of these proteinase inhibitors have been shown *in vitro* to lighten skin pigmentation and are found in a variety of moisturizers.<sup>12</sup> In addition, the Bowman-Birk inhibitor has been shown to reduce hair growth and is found in aftershave moisturizers to prevent hair regrowth. Human studies on final cosmetic formulations to both lighten skin pigmentation and reduce hair growth have not been conducted, making the topical effects of soy less documented than the oral benefits.

Based on the published work on the benefits of soy consumption in the nutrition sciences literature, I decided to study an oral soy supplement in conjunction with another physician-research scientist involved in manufacturing a soy supplement. This soy supplement was a powder added to water, juice, or milk to create a shake rich in flavonoids, including genistein, diadzein, and glycitein. The supplement contained 20 g of soy protein with 160 mg of isoflavones.

## Method

The pilot study enrolled 40 women, 50 to 65 years of age, with mild to moderate photoaging. These patients had entered menopause naturally and had not experienced a menstrual cycle for more than 12 months. At the time of the study, the women were not taking oral soy supplements, consuming soy-containing foods, or on hormone replacement therapy. Twenty subjects were randomized to receive the soy supplement in addition to their normal

self-selected diets for 6 months, and 20 continued on their self-selected diets for 6 months. The randomization groups were blinded to the investigator and balanced for age, degree of photoaging, and investigator-rated assessment of skin, hair, and nail appearance. The subjects were asked to come into the office for examinations at 3 and 6 months and to maintain a food diary. At each visit, the subjects completed a questionnaire detailing their perception of skin, hair, and nail appearance. Damage to the skin, hair, and nails was assessed on a scale of 0 (none) to 4 (severe). A visual investigator assessment was also completed. Photography, transepidermal water loss, and corneometric measurements were also collected.

Facial skin was assessed for roughness, wrinkling, flaking, discoloration, and overall appearance. To standardize the effects of cosmetics on the hair and nails, subjects were asked to use a shampoo from an approved list. Hair appearance was evaluated by assessing roughness, dullness, lack of manageability, and scalp flaking. Subjects were asked to not use nail polish or nail prostheses during the study so that nail roughness, ridging, flaking, and splitting could be assessed.

## Pilot Study Results

The results for the pilot study on soy supplements revealed many physical benefits. At the end of 3 months, statistically significant investigator-assessed improvement was noted in facial-skin flaking ( $P=.028$ ), discoloration ( $P=.045$ ), and overall appearance ( $P=.05$ ) in the soy supplement group. At the end of 6 months, investigator-assessed improvement was noted in the soy supplement group in facial-skin wrinkling ( $P=.004$ ), discoloration ( $P=.016$ ), and overall appearance ( $P=.0001$ ).

Investigator-assessed improvement in hair appearance was noted in the soy supplement group at both the 3-month and 6-month evaluations. Improvement was noted in hair roughness ( $P=.041$ ), manageability ( $P=.018$ ), and overall appearance ( $P=.016$ ) at the end of 3 months. Additional improvement was noted at the end of 6 months in hair roughness ( $P=.004$ ), dullness ( $P=.048$ ), and overall appearance ( $P=.005$ ).

Investigator-assessed improvement of appearance was noted in the nails of the subjects in the soy supplement group. No changes were noted at the end of 3 months; however, by the end of 6 months, improvement was noted in nail roughness ( $P=.017$ ), ridging ( $P=.006$ ), flaking ( $P=.049$ ), splitting ( $P=.007$ ), and overall appearance ( $P=.008$ ).

The subjects in the soy supplement group perceived improvement in facial-skin roughness ( $P=.013$ ) and wrinkling ( $P=.014$ ) at the end of 3 months. There was

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a continued perception of improvement in facial-skin roughness ( $P=.009$ ) at the end of 6 months; however, the subjects did not perceive any differences in the appearance of their hair or nails after 3 months. Some subjects noted improvement in hair roughness ( $P=.037$ ) after 6 months but no improvement in nail appearance.

The noninvasive transepidermal water loss and corneometric measurements did not show any statistically significant differences in skin moisturization at 3 months or 6 months.

## Summary

This preliminary pilot study demonstrated some interesting findings on using soy in skin, hair, and nail health. Soy is a rich source of protein and phytoestrogens. Since the skin, hair, and nails are primarily composed of protein, it is possible that providing a regular dietary protein source may improve the appearance of these body structures in postmenopausal women who may not be self-selecting a diet with sufficient protein. Furthermore, oral administration of phytoestrogens may have a beneficial effect on appearance in postmenopausal women who do not use estrogen hormonal supplementation. There is no doubt that estrogen has a profound effect on the skin, hair, and nails, yet our understanding of how to supplement estrogen in postmenopausal women is poor. Clearly, this work on soy is preliminary, but it may be that oral soy supplementation has a role in dermatology for postmenopausal women.

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