"Bust Enhancing" Herbal Products

Adriane Fugh-Berman, MD

Department of Health Care Sciences, George Washington University School of Medicine, Washington, DC

"Bust enhancing" herbal products are widely advertised. No clinical trials have been published. These products contain a variety of ingredients, including grains, hops, saw palmetto, dong quai, chaste-tree berry, wild yam, kava, fennel, black cohosh, and fenugreek. Several of these herbs are hormonally active; for example, hops contain 8-prenylnaringenin, a phytoestrogen that is more potent than other dietary phytoestrogens. Many bust-enhancing dietary supplements contain substrates for *Fusarium,* a fungus that produces zearalenone, a potent estrogen that has been associated with breast enlargement in humans and other species. The use of bust-enhancing products should be discouraged because of lack of evidence for efficacy and long-term safety concerns. (Obstet Gynecol 2003;101: 1345–9. © 2003 by The American College of Obstetricians and Gynecologists.)

"Bust enhancing" dietary supplements are widely marketed to young women. A typical product costs $229 for an 8-week supply. These products contain variable combinations of herbs, the most popular being hops *(Humulus lupulus),* saw palmetto *(Serenoa repens),* damiana *(Turnera diffusa),* dong quai *(Angelica sinensis),* chaste-tree berry *(Vitex agnus-castus),* blessed thistle *(Cnicus benedictus),* dandelion *(Taraxacum officinale),* wild yam *(Dioscorea villosa),* kava *(Piper methysticum),* fennel *(Foeniculum vulgare),* black cohosh *(Cimicifuga racemosa),* and fenugreek *(Trigonella foenum-graecum).* Some products also contain cereal grains, including barley and oats. Here I review available evidence on the efficacy and safety of purported bust-enhancing products. The databases MEDLINE (1966–2002), TOXLINE (1972–2002), and REPROTOX were searched broadly using the following key words: "bust enhancers," "breast enlargement," "mammoplasia," "gynecomastia," *"Fusarium,"* "zearalenone," "zearalenol," "8-prenylnaringenin," and the names of the individual herbs and grains listed above. Information from this search was supplemented from the author's extensive files.

Address reprint requests to: Adriane Fugh-Berman, MD, 1312 18th Street NW, Washington DC 20036; E-mail: fughberman@aol.com.

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HUMAN AND ANIMAL STUDIES

No clinical trials on the efficacy of bust-enhancing dietary supplements have been published or presented to the scientific community. The popularity of these products stems from promotion on television, on the Internet, and in magazines aimed at young women. Testimonials are heavily used. An episode of the television show *20/20* on bust-enhancing products (aired June 21, 2002) revealed that filmed testimonials were from paid actors, and suggested that differences shown in "before and after" pictures could be accounted for by lower-cut clothing and pushup bras.

No animal studies have examined the effect of bust-enhancing products or their constituents on mammary glands. Two estrogenicity assays of these products in rodents were identified.[1,2] One showed no estrogenic effect on the uterus, whereas the other showed only small and inconsistent effects. The first study tested Erdic (Erdic International, London, United Kingdom) (also sold as "Busting Out"), a product based on grains and hops.[1] The composition of this product has changed over time. The current ingredients are "hops, buckwheat, fennel, rye, malt, barley, and L-ornitine [sic]"[3]; the package of a product purchased in 1999 states that it contains "barley, hops (2 sorts), rye, wheat, malt, black oats, maize." It is not clear which formulation was tested. Twenty female Sprague–Dawley rats from four dams (litters were reduced to ten pups per dam) were randomly distributed to three groups of six weanlings each. Controls consumed a soy-free diet (AIN-93), positive controls consumed the same diet with 160 μg of estradiol 3-benzoate, and the third group received a 20% powdered Erdic, 80% AIN-93 diet for 3 days. There were no differences in uterine weights among the Erdic and control groups. Mean body weights were similar among groups.

The second study, in mice, tested an herbal "bust enhancement" product (not otherwise identified) containing significant amounts of hops phytoestrogens.[2] Fourteen day 18 mice were injected subcutaneously with 0.1 mL of an extract of the supplement or 17α-ethinyl estradiol dissolved in corn oil. Animals were killed on day 4. Ovariectomized adult mice (seven per group) received feed containing either 17α-ethinyl estradiol or

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the herbal supplement in feed (1:1, 1:9, and 1:99 weight/weight) for 5 days and were killed on day 6. In the prepubertal mouse uterotrophic bioassay, the dietary supplement significantly increased the uterus/body weight fraction at two of five doses in a non–dose dependent manner (0.24 and 0.84 μg of 8-prenylnaringenin, but not 0.024, 0.084, or 2.4 μg of 8-prenylnaringenin). In the ovariectomized mouse uterotrophic bioassay, the dietary supplement significantly reduced the uterine/body weight fraction in only the lowest of three doses (at a ratio of 1:99, but not 1:9 or 1:1). Oral dosing significantly decreased uterine weight in mice only at the lowest dose tested (13.6 ng of 8-prenylnaringenin/g) and not in a dose-dependent manner. 17α-ethinyl estradiol significantly increased the uterine/body weight fraction relative to controls in both bioassays. The researchers concluded that the supplement has only weak effects on the uterus even with oral doses containing 542 ng/g of 8-prenylnaringenin, representing a dose 258-fold higher than expected daily intake of the product.

ESTROGENICITY STUDIES IN INDIVIDUAL HERBS

Hops *(Humulus lupulus)*

Several herbs used in these formulas have been tested for estrogenic effects. A common ingredient in bust-enhancing formulas, hops (*Humulus lupulus* L.) contain the phytoestrogen 8-prenylnaringenin. Beer is flavored with hops and may contain 8-prenylnaringenin, but beer has not been specifically linked to breast enlargement.[4] Anecdotally, female hops pickers have developed menstrual irregularities[5] (8-prenylnaringenin apparently can be absorbed via the skin). The scientist who isolated 8-prenylnaringenin from hops credits his interest in the field to his wife's development of menstrual irregularities after working with hops.[6]

A small, methodologically flawed study found a benefit of 30 days of treatment with large doses of hops extract (1600–2600 mg per day, titrating down to 1200–1600 mg) on hot flashes in 25 women.[7] The study was not randomized, and the control group was apparently composed of five women who had been accidentally treated with a low dose of hops (300 mg), which because it showed no benefit was considered a placebo. In 17 of 20 treated subjects, reduction of hot flash score (intensity × frequency) was significantly better than in controls; neither statistical test nor significance level was stated. Some subjects apparently received another herb, hawthorn (*Crataegus* sp), as well as hops.

8-prenylnaringenin has 0.2–20% of the potency of estradiol.[3] Other hops phytoestrogens, including 6-prenylnaringenin, 6,8-diprenylnaringen, and 8-geranylnaringenin, are also estrogenic, but have only 1% of the potency of 8-prenylnaringenin.[8] 8-prenylnaringenin binds equally to α and β estrogen receptors.[9] A study of 8-prenylnaringenin, administered subcutaneously, found that 30 μg/g per day caused uterotrophic effects in ovariectomized rats.[9] 8-prenylnaringenin was more potent than coumestrol, genistein, or daidzein in several assays, including stimulation of alkaline phosphatase in Ishikawa Var I cells and competitive displacement from rat uterine cytosol by [2,4,6,7-3H]17β-estradiol).[10] In ovariectomized mice, 100 μg of 8-prenylnaringenin/mL (about 15 mg/kg per day) caused an estrogenic mitotic response in vaginal but not endometrial epithelium.[4]

Black Cohosh *(Cimicifuga racemosa)*

It is unclear whether or not black cohosh, currently a popular treatment for hot flashes, has an estrogenic effect. Clinical studies are mixed, but some show a benefit of black cohosh for treating hot flashes or improving the vaginal maturation index; it does not appear to affect prolactin, estradiol, sex hormone–binding globulin, luteinizing hormone (LH), or follicle-stimulating hormone (FSH) levels in humans.[11] Even if black cohosh is effective for treating hot flashes, this is not necessarily an estrogenic effect.

Formerly thought to contain the phytoestrogen formononetin, black cohosh has not been found to contain formononetin in recent studies.[12] It does contain small amounts of a recently identified phytoestrogen, fukinolic acid[13] (2E-caffeoylfukiic acid), which has shown estrogenic activity in a breast cancer cell line and increased uterine weight in rats.[13] It is difficult to extrapolate from the activity of an isolated constituent to use of the whole herb, especially when the constituent is present in tiny quantities. In vivo and in vitro estrogenicity studies of black cohosh are mixed. Increased uterine weight was seen in two studies of mice given black cohosh[14] (Eagon CL, Elm MS, Teepe AG, Eagon PK. Medicinal botanicals. Estrogenicity in rat uterus and liver [abstract]. Proc Am Assoc Cancer Res 1997;38:293); two other studies showed no estrogenic effects in mice given oral doses[15,16] or rats given injected doses.[16] A recent test of black cohosh in several in vitro assays for estrogenicity showed no estrogenic activity.[17]

Dong Quai *(Angelica sinensis)*

Dong quai, a Chinese herb used in many women's health formulas, has been tested for hot flashes in a randomized, double-blind clinical trial; there was no effect on hot flashes, vaginal mucosa, or endometrium.[18] The herb is not considered estrogenic in traditional Chinese medicine. There is one report of dong quai–associated gynecomastia (breast enlargement in males) in a man in Singapore.[19] This appears to be an isolated

case, and the product was not analyzed; it may have been adulterated with drugs.

Fennel *(Foeniculum vulgare)*

Little information is available on fennel seed, used as both a culinary and a medicinal herb, but one animal study found an estrogenic effect. In female rats, oral administration of an acetone extract of fennel seed (dose not available in abstract) for 10 days caused vaginal cornification and estrus.[20] Moderate doses increased the weight of mammary glands; higher doses increased the weight of the oviduct, endometrium, myometrium, cervix, and vagina.

OTHER HORMONAL EFFECTS

Kava *(Piper methysticum)*

Kava appears to have dopamine antagonist effects.[21] Dopamine antagonists increase prolactin secretion, and increased prolactin may be associated with mammoplasia (breast enlargement in women). Selective serotonin reuptake inhibitors can increase prolactin levels, and an observational study in 59 women treated with selective serotonin reuptake inhibitors or venlafaxine for more than 2 months found that 23 of them (39%) reported some mammoplasia.[22]

Saw Palmetto *(Serenoa repens)*

Saw palmetto, used primarily to treat benign prostatic hypertrophy, inhibits binding of dihydrotestosterone to androgen receptors in prostate cells and inhibits binding of [3H]dihydrotestosterone to its receptor in human foreskin fibroblasts.[23] Saw palmetto also inhibits prolactin[24] and has potent α_1-adrenoceptor effects in vitro.[25] Studies are mixed on whether or not saw palmetto inhibits 5α-reductase.[26–28] An antiestrogenic effect was noted in men with benign prostatic hyperplasia who received *Serenoa repens* (160 mg twice a day).[29] These effects would not be expected to enlarge breasts.

Chaste-Tree Berry *(Vitex agnus-castus)*

Vitex decreases FSH and increases LH, and inhibits prolactin activity in vitro.[30] None of these effects should be associated with mammoplasia.

Fenugreek *(Trigonella foenum-graecum)* and Wild Yam *(Dioscorea villosa)*

Although roasted fenugreek seeds were reputedly used by harem women to enhance buxomness,[31] there is no evidence that fenugreek increases breast size. Both fenugreek and wild yam contain diosgenin, which can be converted to progesterone in a laboratory, but there is no evidence that such conversion takes place endogenously. An article distributed as evidence that diosgenin increases mammary size does not support the claim. This experiment, in which 20- or 40-mg/kg diosgenin was given with or without estrogen to ovariectomized mice, found no difference in wet or fat-free dry weight of mammary glands in diosgenin-treated mice.[32] Diosgenin did significantly affect mammary maturation, increasing terminal end bud differentiation (an effect that takes place in late pregnancy or under estrogen treatment). Although the words "growth stimulator" and "mammary development" are used, in this case maturation is what is meant.

ADVERSE EFFECTS OF BUST-ENHANCING HERBS

No adverse effects of the most common bust-enhancing herbal products were apparent on the US Food and Drug Administration Special Nutritionals Adverse Event Reporting System (accessed August 2002). Kava has been associated with numerous cases of hepatotoxicity and should not be used[33]; acute dystonic reactions have been reported as well. Dong quai has been associated with increased risk of bleeding when combined with anticoagulants.[34] No serious adverse events have been associated with black cohosh, saw palmetto, fennel, damiana, blessed thistle *(Cnicus benedictus),* or dandelion *(Taraxacum officinale)*.

Most of the ingredients in these products have not been associated with significant adverse effects. Estrogenic stimulation of breast or endometrial tissue is of concern with long-term ingestion of hormonally active compounds; however, data to date do not support potent hormonal effects of the labeled ingredients in bust-enhancing products.

COULD THESE PRODUCTS BE EFFECTIVE?

No clinical trial of a bust-enhancing herbal product has been published. It is unlikely that any of these products, if they contain what their labels say that they contain, would cause breast enlargement. Drugs associated with gynecomastia or mammoplasia include estrogen, protease inhibitors, penicillamine, neuroleptics, and antidepressants (including tricyclics, monoamine oxidase inhibitors, and serotonin reuptake inhibitors).[35] No cases of gynecomastia or mammoplasia have been reported for herbs or grains except for a single unreliable case of gynecomastia associated with dong quai (the product was not analyzed to exclude steroid adulteration, which is not uncommon in Asian herbal medicine products). Some herbs contain estrogenic compounds, but the phenolic phytoestrogens found in plants would not be expected to be potent enough to cause mammoplasia. Kava

has dopamine antagonist qualities and could raise prolactin levels, but this effect has not been demonstrated and would be unlikely to be strong.

The labeled ingredients in bust-enhancing products are unlikely to enlarge breasts. However, some bust-enhancing products contain hops or grains that are excellent substrates for *Fusarium,* a mold that commonly infests cereal grains. *Fusarium* spp produce zearalenone, an anabolic, potent resorcyclic acid lactone phytoestrogen. *Fusarium* has been identified in corn, wheat, barley, malt, rye, oats, and beer (which contains hops).[36] Sprouting, or "malting" barley (an excellent substrate for *Fusarium*) increases the zearalenone concentration 50-fold.[37]

Zearalenone from moldy feed affects the reproductive organs of animals. Male and female pigs given moldy feed contaminated with *Fusarium* suffer mammary enlargement and other symptoms.[37] Humans may also be affected. *Fusarium*-contaminated grain was linked to "endemic breast enlargement disease" in China.[38] It was later determined that all samples of buckwheat grown in the area were infected with mold; 34% were infected with *Fusarium*.[39] Zearalenone was extracted from the affected buckwheat.

There is no evidence that bust-enhancing products are contaminated with *Fusarium*. However, to my knowledge only one product has been tested. A high-pressure liquid chromatography analysis of an Erdic product purchased in 1999 revealed no zearalenone or α-zearalenol (unpublished data, E. Kennelly, F. Kronenberg, A. Fugh-Berman). It would be enlightening to analyze the plethora of available products for the presence of zearalenone or zearalenol.

CONCLUSION

There is no published evidence for efficacy of bust-enhancing herbal supplements. Products marketed for "bust enhancement" contain herbs that may have pharmacological effects. There are no long-term safety data on any of these herbs, singly or in combination. Some products contain substrates for *Fusarium,* a zearalenone-producing fungus associated with breast enlargement in humans and pigs. Physicians should discourage the ingestion of pharmacologically active substances with unknown safety risks for the purpose of breast enlargement.

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