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## Soy and Menopausal Symptoms

*By Monica J. Stokes, MD, FACOG, ABHM*

MENOPAUSE CONSISTS OF A WIDE VARIETY OF SIGNS AND SYMPTOMS associated with acute withdrawal, or natural fluctuation and eventual diminution, of female reproductive hormones. This is superimposed on a background of progressive changes associated with aging. Medical problems may be initiated or exacerbated by withdrawal of the hormonal milieu associated with the reproductive age range.

Most animal and human studies regarding the health effects of soy are difficult to compare due to differences in the type of soy products used and the amount of isoflavone present. Despite this, it is clear that regular consumption of soy during the menopausal period may be helpful for some of the typical symptoms encountered. The use of soy beginning early in life or during early menopause also may be helpful for the prevention (and possibly the adjunctive treatment) of medical issues such as osteoporosis, some aspects of cognitive dysfunction, cardiovascular disease, and some cancers that may affect aging women.

Studies are ongoing to assess soy's nutritional profiles and possible health effects in animals and humans.<sup>1</sup> In addition, investigations are elucidating soy's phytochemical pharmacokinetics and bioavailability,<sup>2</sup> which should help determine which sources, purified extracts or food sources, will convey which specific benefits. Ultimately, these investigations will coalesce to determine which combination of constituents in soy exert which health benefits, and which individuals are likely to benefit most.<sup>3</sup>

### Constituents

In addition to soy protein, soy is a major source of the isoflavone class of phytoestrogens, consisting primarily of daidzein and genistein. It is thought that isoflavones act as weak estrogens, reversibly binding to estrogen-receptor isoform beta (ER- $\beta$ ) with greater affinity than estrogen-receptor alpha (ER- $\alpha$ ). Isoflavones have been compared to selective estrogen-receptor modulators, in that they exert estrogen-like activity in some tissues, and no effect or anti-estrogenic activity in other parts of the body. ER- $\beta$  receptors seem to be expressed more than ER- $\alpha$  in the central nervous system, the

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cardiovascular system, bone, and skin. ER- $\alpha$  receptors are in greater predominance in the uterus and breast. Isoflavones also may act via a number of non-hormonal mechanisms.

## Equol

Equol was first identified in human urine in the early 1980s.<sup>4</sup> Since that time, this metabolite of the isoflavone daidzein has demonstrated a more potent estrogenic potential than its precursor.<sup>5</sup> There is considerable inter-individual variability in the metabolism of isoflavones including that of this bioactive, gut metabolite.<sup>6</sup> Increased urinary excretion of equol in premenopausal women has been associated with a reduced risk of breast cancer.<sup>7</sup> Equol excretors (equol-producers encompass about 45% of women) display different (favorable) plasma hormone profiles in comparison to non-excretors (non-producers). Equol excretor status may explain the variance regarding the biomarker and health benefits of soy in previous studies that did not consider this influence. Future isoflavone studies will likely control for this confounder. It will not be surprising if other bioactive metabolites of soy are identified in the near future.

## Vasomotor Symptoms

The data regarding the benefit of soy for hot flashes and night sweats are mixed. Several studies have shown no benefit.<sup>8</sup> The Soy Estrogen Alternative Study found no significant differences between soy protein alone or soy protein with two different moderate doses of isoflavones over a two-year period.<sup>9</sup> This study chose perimenopausal women (likely having wide endogenous hormonal fluctuations affecting their symptom frequency), most with fewer than five hot flashes in a day, and more than 50% of the participants had previously used estrogen therapy, albeit more than three months before entering the study. The majority of studies, however, support a trial of soy foods or comparably dosed isoflavone extract supplements for the treatment of hot flashes and night sweats.<sup>10-12</sup> In general, the expected degree of benefit is directly related to the degree of pre-treatment hot flash frequency.<sup>13</sup>

In January 2004, the North American Menopause Society (NAMS) published a position statement on the treatment of menopause-associated vasomotor symptoms.<sup>14</sup> Of the 15 randomized, double-blind (mostly placebo-controlled) trials reviewed in a section on isoflavones, only four studies demonstrated a significant decrease in hot flashes. Although acknowledging that the studies are difficult to compare due to differences in soy products used, and that the data on the estrogenicity of isoflavones are inconclusive, NAMS concluded that the potential for adverse effects is minimal with isoflavones from isoflavone isolates or food sources in the 40-80 mg/d dose range. (Interestingly, an individual's intestinal equol production capacity does not appear to correlate with the degree of reduction of hot flash frequency obtained with soy consumption.)

In postmenopausal breast cancer survivors, Van Paten et al found that consumption of a soy beverage containing 90 mg of isoflavones over 12 weeks was no better than placebo in reducing the frequency of hot flashes.<sup>15</sup> In a crossover trial using 114 mg/d of isoflavones in a similar population, similar results were obtained even when controlling for equol level status.

## Vaginal Atrophy Prevention

In studies evaluating soy intake and improvement in vaginal cellular maturation index measurement as primary<sup>16</sup> or secondary<sup>17,18</sup> outcome, the results remain mixed with most studies finding no change during study periods of six months or less.

## Osteoporosis: Soy and Ipriflavone

Soy foods and soy protein with and without isoflavones of varying doses continue to be studied to

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## Questions & Comments

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determine their role in the prevention and treatment of osteopenia and osteoporosis. High soy protein dosing, in contrast to high doses of animal protein, may have a less pronounced effect on renal calcium excretion, most likely related to an insulin-modulating effect on the kidney.<sup>19,20</sup> Daidzein and genistein both suppress osteoclast activity, and genistein has been noted to have a stimulatory effect on osteoblasts in vitro as well as an anabolic effect on bone in animal models.<sup>21</sup> Studies have produced conflicting reports on the effects of varying doses of isoflavones on markers of bone turnover.<sup>22</sup> Collective data from in vitro, in vivo, human observational, and dietary intervention studies<sup>23</sup> suggest that diets rich in phytoestrogens have bone-sparing effects in the long term. Soy isoflavones may offer the maximum benefit as a preventive intervention, not as a treatment for osteopenia and osteoporosis.

Ipriflavone is a synthetic derived from soy isoflavones. One ipriflavone metabolite, daidzein, undoubtedly contributes to its bone-sparing capacity (*see* Alternative Medicine Alert, *December 2000*). Ipriflavone has been found to have antiresorptive and possibly mild stimulatory effects on bone in the treatment of osteopenic and osteoporotic postmenopausal women (following urinary n-linked telopeptides, bone mineral density, and other measures of bone turnover, but few reported fracture endpoints).<sup>24</sup> The bone-sparing effect is noted primarily at the lumbar spine, but has been shown to affect radial bone and femoral neck density as well. It has been shown to minimize glucocorticoid-<sup>25</sup> and GnRH agonist-induced<sup>26</sup> bone mass loss.

Ipriflavone currently is not recommended for use in pregnant or lactating women. It is to be used with caution in those with liver or kidney disease,<sup>27</sup> and by those using theophylline (increased risk of toxicity).

A recently published, prospective four-year, randomized, double-blind, placebo-controlled multicenter study reported that ipriflavone may induce a slowly reversible lymphocytopenia in some patients.<sup>28</sup> Renal and hepatic function, as well as lymphocyte counts (especially neutrophils), should be monitored during the first 6-12 months of treatment. The long-term effects of this dosing on the breast and female genital tract are as yet unknown.

The most common dosing of ipriflavone in published studies is 200 mg three times daily. The greatest bone-sparing benefit is obtained when taken concurrently with 1,000 mg/d of elemental calcium and 400-800 IU/d of supplemental vitamin D.

### **Cognitive Function**

Genistein has been found to be comparable to 17 $\beta$ -

estradiol in its anti-apoptotic properties on models of primary cortical neurons (rich in ER- $\beta$ ).<sup>29</sup>

The longest-running published trial was the Soy and Postmenopausal Health In Aging (SOPHIA) study, a methodologically sound study that looked at 56 cognitively intact women aged 55-74 years who were at least two years postmenopausal and not using hormone replacement therapy.<sup>30</sup> The subjects were given 110 mg (a relatively high dose given divided in two daily doses) of extracted soy isoflavones or placebo daily for six months. The treatment group improved not only against their own baseline cognition scores, but were consistently better than the placebo group, especially in the area of verbal memory. As with estrogen administration, it is likely that the role for soy isoflavones is preventive, not therapeutic, in the maintenance of intact cognitive functioning during the aging process.

### **Cardiovascular Health**

Heart disease remains the No. 1 cause of death in postmenopausal women. Despite this, public health messages (similar to efforts surrounding breast cancer awareness) regarding this fact have only very recently become more apparent in the media. Early, healthy dietary habit development and dietary interventions are two preventive strategies that must be employed to reduce the incidence of cardiovascular disease in women. Dietary soy certainly has a place in this effort.<sup>31</sup>

Soy isoflavones have been found to improve plasma lipids even in normocholesterolemic, premenopausal women throughout the menstrual cycle.<sup>32</sup> Garcia-Martinez et al found that endothelial culture cells increase their ability to produce prostacyclin when treated with serum from postmenopausal women treated with isoflavones from soy and red clover.<sup>33</sup> Steinberg et al found that daily consumption of soy protein with isoflavones had positive effects on vascular reactivity independent of lipid and antioxidant effects in healthy postmenopausal women.<sup>34</sup>

In a meta-analysis of 38 controlled clinical trials (men and women), Anderson et al examined the relation between soy protein containing isoflavones (25-50 g/d equivalent to 2-5 servings of soy foods per day) vs. animal protein consumption and serum lipids in humans.<sup>35</sup> The authors concluded that significant reductions in total cholesterol, LDL-cholesterol, and triglycerides occur with soy but not animal protein, with the most profound effects noted in those subjects with the highest baseline levels. No significant changes in serum HDL-cholesterol levels were reported.

In October 1999, the Food and Drug Administration approved a food label health claim for reduced risk of

heart disease on foods containing 6.25 g of soy protein per serving, assuming four servings, or 25 g of soy protein intake daily. Concurrently, the American Heart Association's Nutrition Advisory Committee upgraded soy protein and isoflavones from its 1993 position, granting it a definite place in a heart-healthy diet, especially when used as a substitute for animal (highly saturated) fats and processed foods.<sup>36</sup> Soy is particularly recommended for high-risk populations with elevated total and LDL-cholesterol. Citing Crouse et al, the American Heart Association recommends avoiding soy foods and concentrates that employ ethanol washing,<sup>37</sup> which depletes isoflavone and possibly other bioactive soy component content, as there appears to be a dose-response effect of isoflavone content in soy and the degree of cholesterol-lowering effect.<sup>38</sup> Due to the increased cardiac risk faced by diabetic postmenopausal women, soy use should be especially encouraged.

### Safety

Low-dose soy supplementation does not appear to alter postmenopausal plasma hormone levels for estradiol, gonadotropins, prolactin, testosterone, sex hormone-binding globulin, or DHEAS.<sup>39,40</sup> However, it has been suggested that even over a short term, soy consumption does appear to modulate endogenous estrogen metabolism in postmenopausal women, leading to a decrease in the ratio of negatively up-regulating and genotoxic estrogen metabolites (i.e., 16- $\alpha$ -hydroxyestrone and 4-hydroxylated catechol estrogens associated with breast cancer) to total estrogen levels. This suggests that soy constituents may exert cancer-preventive effects in postmenopausal women.<sup>41</sup> Pharmacokinetic studies with huge single-dose administrations of purified soy isoflavones to postmenopausal subjects demonstrated that progressive accumulation with chronic dosing is unlikely.<sup>42</sup>

Genistein has been found to have a biphasic effect on the growth of MCF-7 cells in vitro with stimulation at low concentrations and inhibition at high concentrations. In animal models, genistein and soy protein have stimulated tumor growth in a dose-dependent manner and inhibited it.<sup>43</sup> The estrogen status of the subject and/or the life-stage timing of administration<sup>44,45</sup> may influence the combined effect of soy administration. The question of whether soy is protective against breast cancer or is harmful for women with a history of or at high risk for breast cancer remains unanswered.

Soy isoflavones, alone, have not been found to increase endometrial thickness.<sup>46,47</sup> High-dose soy administration, as might be expected, does not act in a protective manner when matched against pharmacologic

dosing of estradiol with respect to the endometrium. In recent randomized, controlled clinical trial (six months),<sup>48</sup> soy protein isolate with 120 mg (high dose) of added isoflavones failed to block the effect of 0.5 or 1.0 mg of exogenous estradiol administration on the development of endometrial hyperplasia commonly associated with unopposed estrogen therapy in postmenopausal women.

### Soy and Thyroid Function

One multi-ethnic, population-based, case-controlled study found that those with the highest quartile of soy-based food intake had the lowest risk for the development of thyroid cancer (odds ratio 0.65).<sup>49</sup>

A 1959 article by Van Wyk et al, in the journal *Pediatrics*, referenced rat data that showed that the goitrogenic effect of soy was blocked by iodine supplementation greater than the (at that time) recommended daily requirement. Since then, animal studies have shown that soy may stimulate T and B cell-mediated immune function. There is early speculation that in the face of certain background factors, such as iodine deficiency or the presence of other goitrogenic dietary (or possible genetic) components, constituents in soy (especially dietary genistein) might induce thyroid autoimmunity via inactivation of thyroid peroxidase.<sup>50</sup> Given the high incidence of subclinical hypothyroidism in older individuals, this should be fertile ground for future study. In the meantime, it would be prudent to re-check thyroid function levels in those individuals with non-ablative hypothyroidism who begin incorporating soy products (regularly) into their diets to be sure no changes need to be made.

### Soy Sources

Available food sources include whole soybeans (fresh or dried), miso, soy protein powder, textured soy protein, soy flour, tempeh, soy meat alternatives, soy milk (often calcium- and vitamin D-fortified), and soy-fortified foods. The more processed the product, the more likely the depletion of the isoflavone content of the soy. While not all soy foods carry the soy protein or isoflavone content printed on their labels, foods that carry the heart health claim allowed by the FDA may now include the isoflavone or soy protein content claimed. In 2001, however, a study of 33 commercial phytoestrogen supplements and extracts revealed that there were considerable differences in the isoflavone content from that claimed by the manufacturers.<sup>51</sup>

In addition, concentrated encapsulated or otherwise powdered soy extracts (purified isoflavone or soy protein and isoflavone) are available; however, patients

must be careful to avoid alcoholic extracts as they deplete the isoflavone content of the product. Patients also should avoid large doses (greater than 100 mg/d) of concentrated, extracted products until more is known about the long-term effects of these isolated products' potential dose-related effects.

Ipriflavone, a synthetic isoflavone derived from the isoflavone classes found in soy, is also available. As described earlier, it has been studied primarily for its use for prevention of bone loss.

### Dosing

Studies cited in this paper have used a range from 20 mg to 125 mg of isoflavones per day. The American Heart Association recommends 25-50 g/d of soy protein with the caveats for avoidance of alcohol-extracted products to be sure the isoflavone content remains intact. Food-sourced consumption of less than 100 mg/d of isoflavones is likely safe in the long term. Patients should avoid excessive dosing with concentrated/extracted products. Pharmacokinetic research suggests that separate servings during the day may be the best way to consume soy protein and isoflavones. It is as yet unclear whether this dosing is completely safe for breast cancer patients or those at high risk; however, one to two daily servings of soy foods is unlikely to be detrimental given current conclusions of research on this subject. For ipriflavone, the studies have used 200 mg three times daily for its bone-sparing effects. Consider the caveats noted previously if recommending its use.

### Conclusion

Although we have many answers regarding soy, we have many more questions including the influence of age-related differences in exposure with health outcomes (perinatal, childhood, peripubertal, adult); timing of dosing with relation to intrinsic estrogenic state; differences in effects in different population groups (ethnic, metabolic, deficiency states, etc.); how to handle the high inter-individual variability in metabolism of isoflavones and of other, yet to be identified soy metabolites, or using these variables to our advantage to predict responses; and optimal dosing for specific health outcomes.

The possible adverse effect of various soy products on thyroid function awaits elucidation. The newer data regarding soy's ability to modulate estrogen metabolism and equol production status are intriguing.

### Recommendation

It seems reasonable to trial a soy protein isolate with isoflavones or soy foods for the treatment of hot flashes

and night sweats in peri- and post-menopausal women. Due to the lack of long-term studies, however, it would be prudent to maintain the daily dose at or below 100 mg of isoflavones per day. It is only logical that whole-food soy sources will contain all of the possible bioactive constituents of soy as compared to extractions of only the currently recognized active factors. For breast cancer patients the safe dose of isoflavones has yet to be elucidated, and for most in this population it does not appear to be helpful for the treatment of hot flashes or night sweats. Until this issue becomes more clear, it would be prudent for women with a history of breast cancer to avoid extracted, non-food soy products, and limit intake to the heart-healthy recommendation level of 25 g of soy protein per day.

For general health, the data seem to support the regular inclusion of soy foods in all of our diets, especially when it is substituted for some of the animal fat and protein so ubiquitous in the Western diet. Dietary soy does not cause the loss of calcium through the urine that animal protein tends to encourage. ❖

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## Goldenseal and the Common Cold: Is There Any Evidence?

By David Kiefer, MD

**G**OLDENSEAL, OR *HYDRASTIS CANADENSIS*, IS A POPULAR cold remedy and immune system stimulant, and combination products with *Echinacea* sp. for this purpose remain a common part of any herbal medicine or dietary supplement shelf at pharmacies and health food stores. In 2000, goldenseal ranked 12th in sales in the natural food trade in the United States,<sup>1</sup> and in 1999, an eight-month estimate of echinacea/goldenseal product sales was \$44.6 million. This was only about 90% of the total market.<sup>2</sup> Such popularity was also enough to earn echinacea/goldenseal products fifth place in herb market sales in 1998.<sup>1</sup> A review for this newsletter in 1998 helped readers sort fact from fiction about this botanical remedy, pointing out the lack of clinical research, and some of the possible side effects associated with using this plant.<sup>3</sup> More research has been done in recent years to help guide physicians and consumers in the correct use of goldenseal.

### History and Traditional Use

Goldenseal is native to North America and was used historically by the Cherokee Indians to treat skin ailments and as an eye wash.<sup>4</sup> Goldenseal also was used traditionally to treat tonsillitis, gastritis, diarrhea, and cystitis; as an oxytocic; and to induce abortions.<sup>5</sup> Early settlers in the United States picked up on the use of goldenseal as a medicine, and it became a popular cure for a variety of gastrointestinal and genitourinary complaints, as well as being an effective bitter tonic.<sup>4</sup> At present, *H. canadensis* most often is used for gastrointestinal infections, and to treat mucous membrane problems of the respiratory or gastrointestinal systems.<sup>6</sup>

In recent years, there has been the rumor that *H. canadensis* in tea form will mask the presence of illicit substances (i.e., opiates, marijuana) in the urine, allowing people to pass drug tests. Scientific investigations into these claims have found no corroborating evidence to substantiate them.<sup>4,7</sup>

### Botany and Pharmacology

*H. canadensis* is a small perennial forest plant of the family Ranunculaceae (Buttercup family). There are numerous isoquinoline alkaloids in the roots and rhizomes (horizontal-growing structures just below the

soil's surface) of *H. canadensis* that are thought responsible for some of its observed physiological effects.<sup>8</sup> The major isoquinoline alkaloids are berberine (which give the herb its characteristic yellow color), beta-hydrastine, canadine, and canadaline.<sup>9</sup> There is some debate about whether these alkaloids are absorbed following oral administration in humans,<sup>4</sup> though it appears that adequate absorption does occur in some animal models.<sup>6</sup>

### Mechanism of Action

The existing research relating to *H. canadensis* is a combination of experiments done using extracts of the crude herb as well as those concentrating on the isoquinoline alkaloid berberine. In vitro studies indicate that berberine has antibacterial and antifungal effects against a variety of microorganisms, including many of the common gastrointestinal pathogens.<sup>1,6</sup> Berberine and two flavonoids found in extracts of the powdered rhizomes of *H. canadensis* displayed antimicrobial properties against the common oral bacteria *Streptococcus mutans* and *Fusobacterium nucleatum*;<sup>10</sup> another in vitro analysis found berberine and beta-hydrastine to be active against *Helicobacter pylori*, though the mechanism of this latter finding is still unknown.<sup>11</sup>

Another study used a 70% alcoholic extract of the rhizomes and roots of *H. canadensis* and tested its bacteriocidal and bacteriostatic activities.<sup>9</sup> The alkaloid hydrastine did not demonstrate antimicrobial activity against any of the strains tested, whereas berberine was active against the gram-positive and gram-negative bacteria tested, except for *Pseudomonas aeruginosa*. Canadine and canadaline were both active against *P. aeruginosa* and most of the other bacteria with specific nuances; canadine did not work against *Escherichia coli*, and canadaline was more effective than berberine against gram-positive bacteria.

One animal study demonstrated that goldenseal caused an increase in the acute primary IgM antibody response to a specific antigen after *H. canadensis* root extract was added to drinking water; there was no change in IgG antibody production.<sup>12</sup> Other animal experiments have shown that berberine also may improve symptoms of diarrhea, decrease intestinal secretion, affect cardiac function, and support in vitro findings of antimicrobial effects.<sup>1,6</sup>

### Clinical Studies

There are no clinical studies investigating the use of *H. canadensis* in the treatment or prevention of the common cold. There have been trials of varying methodological quality on the use of berberine (not the crude herb goldenseal) in humans to treat diarrhea, cholera,

giardia, liver cirrhosis, trachoma, cutaneous leishmaniasis, and diabetes.<sup>5,6</sup> One researcher pointed out that it is problematic to extrapolate studies on berberine to the use of extracts of whole *H. Canadensis* because it is difficult to consume enough hydrastis to achieve the amounts of berberine necessary for therapeutic effects.<sup>5</sup>

### Dosages and Forms

The roots and rhizomes of *H. canadensis* are the plant parts used medicinally. There is a wide variety of recommended dosages for products made from *H. canadensis*. One recent study used 1.53-3.0 g per day of dried rhizomes in divided doses as their standard;<sup>13</sup> this was based on one textbook,<sup>14</sup> and agrees with other reputable sources stating the dosage range as being 500-1,000 mg three times a day.<sup>4,15</sup> Tinctures and extracts often are dosed at 2.0-4.0 mL of 1:10 tincture in 60% ethanol three times a day, or 0.3-1.0 mL of 1:1 liquid extract in 60% ethanol three times a day.<sup>15</sup>

A recent study examined the stated content on the labels of 10 commonly used herbal medicines,<sup>13</sup> and compared the content listed to the recommended dosage amounts in a popular textbook.<sup>14</sup> For the goldenseal part of the study, the range of strengths listed varied by a factor of 20, and only 36% of the products surveyed were consistent with the textbook's standard in both ingredients and dosage. The results of this study illustrate but one of the challenges to consumers and physicians in interpreting the correct dosage regimen of herbal medicines available in the U.S. market, and reinforces the importance of carefully reading labels and comparing the listed contents with reputable sources.

A further confounding factor is the fact that goldenseal products may be adulterated by less expensive, more easily obtainable plants such as Oregon grape (*Berberis aquifolium* or *Berberis nervosa*).<sup>3,5</sup> Though Oregon grape also contains berberine, this herb has a different phytochemical profile and may have different physiological functions as compared to pure goldenseal products.

The U.S Pharmacopeial Convention (USP) represents an effort at the standardization and quality control of herbal products, and their recommendation is that goldenseal root should contain no less than 2.5% berberine and 2.0% hydrastine calculated on a dried basis.<sup>16</sup>

### Conservation

*H. canadensis* is listed under Appendix II of CITES, or the Convention in Trade in Endangered Species.<sup>17,18</sup> This designation requires permits from the U.S. Fish and Wildlife Service for any exports of goldenseal roots or rhizomes. Furthermore, *H. canadensis* currently is listed

as “At Risk” by the United Plant Savers, a non-profit education corporation whose “... mission is to protect native medicinal plants of the United States and Canada and their native habitat while ensuring an abundant renewable supply of medicinal plants for generations to come.”<sup>19</sup> A plant is “At Risk” if it is a medicinal plant in active commerce, its population is dwindling within its current range, and it is rare or sensitive. Due to concerns about the threatened status of wild populations of *H. canadensis*, most herbal medicine experts recommend only using products made from cultivated goldenseal, or switching to other more abundant berberine-containing plants such as barberry (*Berberis vulgaris*).<sup>6</sup>

### **Adverse Effects, Contraindications, and Drug Interactions**

*H. canadensis* may cause a toxic reaction in humans, inducing symptoms such as nausea, vomiting, elevated blood pressure, convulsions, and respiratory failure after ingesting unspecified “large” doses.<sup>7</sup> Others note that diarrhea and vasoconstriction may result from high doses and prolonged use.<sup>20</sup> Isolated berberine in humans may cause cardiac damage, dyspnea, and hypotension in large doses; such toxic doses may occur with 500 mg or more of berberine, and one estimate of the LD<sub>50</sub> for goldenseal is 27.5 mg/kg.<sup>15</sup> Animal studies have shown respiratory and cardiac depression, and stimulation of the gastrointestinal system in large doses, and the opposite effect in lower doses.<sup>15</sup> For these reasons, goldenseal is not recommended for people with hypertension, cardiovascular disease, or respiratory problems. Interestingly, however, recent data suggest a potential benefit of berberine for people with congestive heart failure.<sup>21</sup>

Topical preparations of goldenseal or other berberine-containing plants may react with ultraviolet light to create free radical oxygen compounds and skin and eye irritation in humans; the researchers discovering this effect note that this may also be the mechanism of action for the antimicrobial effect of topical goldenseal preparations.<sup>22</sup>

It is recommended that berberine-containing plants (such as goldenseal) be avoided in pregnancy due to possible uterine stimulant effects, and the fact that berberine can displace bilirubin from serum albumin, which may lead to neonatal jaundice.<sup>4,23</sup> Other contraindications mentioned in the literature include kidney disease (goldenseal alkaloids may accumulate), acute gastric inflammation (goldenseal induces acid production), and high blood pressure.<sup>23</sup>

In vitro studies have shown that the berberine alkaloids present in goldenseal may potentiate the activity of certain medications, including penicillin, chloromycetin,

pentobarbital, and isoproterenol.<sup>22</sup> It is possible that these herb-drug interactions are mediated through the cytochrome P450 (CP450) enzyme system; researchers have demonstrated that a 70% ethanol extract of goldenseal tea is capable of inhibiting several isoforms of the CP450 system,<sup>24</sup> a finding consistent with a past study documenting the inhibitory effects of herbal extracts, tinctures, and pure plant compounds on the CP450 3A4 system.<sup>25</sup>

Berberine has been shown to up-regulate the multi-drug resistant transporter (pgp-170) in two in vitro models.<sup>26,27</sup> This is the same gene product that can cause Paclitaxel, or taxol, to be less effective as an anticancer agent. It would be prudent to recommend to patients taking taxol or other drugs affected by this transporter system to be wary of ingesting berberine-containing plants.

### **Conclusion**

Goldenseal (*H. canadensis*) is a plant native to North America with both present and past uses of its roots and rhizomes as a medicine. There are interesting in vitro studies documenting efficacy as an antimicrobial; however, most of the research was conducted using the isolated alkaloid berberine, the primary alkaloid in goldenseal. There are no clinical studies relevant to its uses as a common cold remedy, and there are a significant number of adverse effects in humans and animals, as well as drug interactions.

### **Recommendation**

Goldenseal is a good example of an herbal medicine whose popular uses as a cold remedy and immune system booster do not coincide with most of the published scientific literature. There are interesting in vitro and animal studies, primarily done on goldenseal’s main alkaloid berberine, that demonstrate a range of effects, including as an antimicrobial and antidiarrheal agent. However, it is unknown how well berberine research results can translate to the use of crude, whole plant extracts of goldenseal. Furthermore, the issues of poor absorption from oral administration, numerous documented side effects and possible drug interactions, a lack of human clinical research for efficacy in treating or preventing the common cold, and goldenseal’s threatened status in the wild, make an effective case for not recommending this plant in most, if not all, clinical scenarios until more evidence accumulates in the literature to guide clinicians in its proper and appropriate use. ❖

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*Dr. Kiefer recently completed a fellowship at the Program in Integrative Medicine, College of Medicine, University of Arizona, Tucson.*

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## Clinical Briefs

With Comments from Russell H. Greenfield, MD

### Acupuncture for Chronic Headache

**Source:** Vickers AJ, et al. Acupuncture for chronic headache in primary care: Large, pragmatic, randomized trial. *BMJ* 2004; 328:744-750.

**Goal:** To compare policies of “use acupuncture” vs. “avoid acupuncture” for people with chronic headaches on headache, health status, days lost from work, and use of resources over one year.

**Design:** Randomized, controlled trial.

**Subjects:** A total of 401 patients with chronic headaches (mainly migraines) were drawn from general practices in England and Wales (data from 301 subjects were included in analysis).

**Methods:** Suitable subjects were identified from within general practices and sent letters describing the study.

Recruitment and screening followed. Twelve separate sites were included, each consisting of a single acupuncture practice together with 2-5 local general practices. Eligible patients completed a four-week headache diary, and were then randomized to “use acupuncture” (usual care plus up to 12 acupuncture treatments over a three-month period), or to “avoid acupuncture” (usual care). Headache severity was recorded four times daily using a Likert scale, while headache score (primary endpoint), SF-36 health status, and medication usage were assessed at baseline, three months, and 12 months. Resource utilization was assessed every three months. One year after randomization, subjects were contacted to provide a global assessment of headache severity, current and baseline, on a scale from 1-10.

**Results:** Mean headache score at 12 months was significantly lower in the acupuncture group than in controls, falling 34% and 16%, respectively. Those randomized to acupuncture used 15% less medication, made 25% fewer office visits, and took 15% fewer days off from work due to illness. Data extrapolation showed that subjects in the acupuncture group experienced 22 fewer days of headache per year compared with members of the control group. SF-36 data revealed superiority of acupuncture over usual care, but only for physical role functioning, energy, and change in health.

**Conclusion:** Acupuncture leads to persistent, clinically important benefits for people with chronic headaches, especially migraines, referred from primary care clinics. Expansion of acupuncture services under the auspices of the NHS should be considered.

**Study strengths:** Close follow-up; diversity of patients; subjects were coached about bias; sample size; only three subjects reported receiving acupuncture outside the study.

**Study weaknesses:** Significant attrition (the authors had anticipated a 25% dropout rate—161/186 completed the

12-month assessment in the acupuncture group, while 140/193 completed the assessment at one year) in the avoid acupuncture group; lack of blinding; no subjects received sham acupuncture.

**Of note:** All acupuncturists in the study had completed at least 250 hours of training and had practiced acupuncture for a median of 12 years; most subjects experienced migraines, with but a small number having tension-type headaches; treatment was individualized to each patient, and subjects received a median of one treatment per week; there was a larger treatment effect in those with more severe symptoms, even after controlling for regression to the mean.

**We knew that:** In an average week, up to 10% of English general practitioners either refer patients for acupuncture or practice it themselves; prior studies have suggested improvements in both severity and frequency of migraine headaches following a course of acupuncture.

**Clinical import:** Despite the increasing availability of effective medical therapy like triptans, many people with migraine headaches continue to experience discomfort that disrupts their daily activities. The situation often leads to a search for viable alternatives, of which acupuncture appears to be one. An article in the same edition of the *BMJ* evaluated the cost of providing such treatment to the chronic headache patients in this study, and found that acupuncture improved health-related quality of life at minimal additional cost. With relative prowess within reach of practitioners after only 250 hours of training, perhaps it is time for more of us to learn this ancient healing art.

**What to do with this article:** Keep a hard copy in your files. ❖

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## Stress and Multiple Sclerosis

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**Source:** Mohr DC, et al. Association between stressful life events and exacerba-

tion in multiple sclerosis: A meta-analysis. *BMJ* 2004;328:731-740.

**Goal:** To further assess the association between exacerbations of multiple sclerosis (MS) and stressful life events.

**Design:** Systematic review and quantitative meta-analysis.

**Studies:** Culled from PubMed, Psych-Info, and Psychological Abstracts from 1965 to 2003.

**Methods:** Three investigators independently reviewed papers, coding studies based on a variety of factors including study design, outcome, type of patients (relapsing-remitting or progressive), and use of validated/unvalidated measures of stress.

**Results:** A total of 20 studies were identified, of which 14 met inclusion criteria (seven case control, seven longitudinal prospective studies). A significant increased risk of MS exacerbation after stressful life events was identified, with a weighted average effect size of  $d = 0.53$ .

**Conclusion:** A modest, but consistent, association exists between non-traumatic stressful life events and subsequent exacerbation of MS.

**Study strengths:** Inclusion of longitudinal prospective trials.

**Study weaknesses:** The unique response of an individual to stress is difficult to control for; weaknesses inherent to meta-analyses including the varying quality of studies; unmeasured factors likely played a role in some of the documented exacerbations.

**Of note:** Charcot first put forth the notion that “grief, vexation, and adverse changes in social circumstance” were related to the onset of MS more than 100 years ago; included studies were statistically homogenous (effect sizes were not impacted significantly by either sampling or study design); the researchers emphatically state that results of this study should in no way

suggest that patients are responsible for their exacerbations.

**We knew that:** The majority of people with MS have relapsing-remitting disease, and most of them believe that stress can cause or contribute to exacerbations; the role of stress as a trigger for exacerbation of MS is controversial among health care providers; at least one other study suggests that traumatic, life-threatening stress may actually reduce the risk of MS exacerbation as compared to more moderate life stresses that can increase exacerbation risk (strongly suggesting that different types of stress create varying physiological

responses); no biological mechanism linking stress and inflammation in MS has yet been tested.

**Clinical import:** The authors of this interesting study refer to a recent meta-analysis of the use of interferon beta for people with MS that showed an overall effect size of  $d = 0.36$  in reducing exacerbations in the first year of treatment, and  $d = 0.30$  over the initial two years of therapy (this compared with an effect size of  $d = 0.53$  associated with stressful life events in this study). While the authors are careful to point out they are not disparaging the use of interferon, they do suggest that the negative effects

of stress may be equivalent to the positive effects of one of the mainstays of treatment of MS, at least as relates to exacerbations.

Although everyone experiences stress, few people can truthfully state that they possess adequate tools with which to manage stress. Health care providers need not wait for additional research to guide people with MS to explore the wide range of stress management techniques readily available to them.

**What to do with this article:** Keep a copy of the abstract on your computer. ❖

## CME Questions

**CME Instructions:** Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

20. The majority of studies support a trial of soy foods or comparably dosed isoflavone extract supplements for the treatment of hot flashes and night sweats.
- True
  - False

21. The bone-sparing effects of ipriflavone have been shown to affect:
- the lumbar spine.
  - radial bone.
  - femoral neck density.
  - All of the above
22. In the Anderson et al meta-analysis, soy protein consumption was associated with significant reductions in all of the following *except*:
- total cholesterol.
  - LDL-cholesterol.
  - HDL-cholesterol.
  - triglycerides.
23. At this time, it would be prudent for women with a history of breast cancer to avoid extracted, non-food soy products, and limit intake to the heart-healthy recommendation level of 25 g of soy protein per day.
- True
  - False
24. Which of the following is among reasons not to recommend the use of goldenseal for the common cold?
- Likely poor absorption from oral administration
  - Numerous side effects and possible drug interactions
  - Lack of efficacy in human clinical research
  - Threatened status in the wild
  - All of the above

Answers: 20. a, 21. d, 22. c, 23. a, 24. e.

## In Future Issues:

**Acupuncture and Low Back Pain**  
**Horse Chestnut and Chronic Venous Insufficiency**  
**Vitamin E and Cardiovascular Disease**  
**Reiki: An Overview**  
**Fenugreek for Hyperlipidemia**

# ALTERNATIVE MEDICINE ALERT™

*A Clinician's Evidence-Based Guide to Alternative Therapies*

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## Soy as Part of a Healthy Diet

THE ARRAY OF SOY FOODS NOW WIDELY AVAILABLE CAN LEAVE SHOPPERS AT A LOSS FOR ways to incorporate them into their diets. However, with the American Heart Association endorsement of soy as a heart-healthy food, more Americans are looking for ways to add this Asian staple into the typical Western diet. This handout describes the more common soy foods and provides nutritional information and storage, cooking, and substitution ideas. For more information and great soy recipes, see [www.soyfoods.com/soybean/sfg03.pdf](http://www.soyfoods.com/soybean/sfg03.pdf).

### Soy milk

**Product Description.** Soy milk is the rich, creamy milk of whole soybeans. It is lactose- and casein-free. Soy milk is available in regular and low-fat varieties, and some brands are fortified with calcium, vitamin D, and/or vitamin B<sub>12</sub>. Soy milk comes in plain, vanilla, chocolate, and strawberry flavors.

**Storage.** Soy milk is most commonly found in aseptic (non-refrigerated) packages, but also is sold refrigerated in plastic or cardboard containers. Unopened, aseptically packaged soy milk can be stored at room temperature for several months. Once opened, soy milk must be refrigerated. It will stay fresh for about five days. Soy milk also is sold as a powder, which must be mixed with water. Soy milk powder should be stored in the refrigerator or freezer.

**Table 1**  
**Soy food protein and isoflavone content**

Soy Food	Serving Size	Soy Protein Content/Serving	Isoflavone Content/Serving
Miso	1 T	2 g	7 mg
Soybeans, green, cooked	1/2 C	11 g	50 mg
Soybeans, black, cooked	1/2 C	9 g	40 mg
Soybeans, yellow, cooked	1/2 C	14 g	78 mg
Soybeans, roasted, plain	1/4 C	15 g	78 mg
Soy milk, plain, unfortified	1 C	7 g	10 mg
Soy milk, plain, fortified	1 C	10 g	43 mg
Soy flour, defatted	1/4 C	12 g	42 mg
Soy flour, full-fat	1/4 C	8 g	33 mg
Soy flour, low-fat	1/4 C	11 g	50 mg
Soy crumbles, meat alternative	1/2 C	11 g	9 mg
Soy protein isolate powder, plain	1/3 C	23 g	53 mg
Textured soy protein, dry	1/4 C	11 g	33 mg
Tempeh	1/2 C	16 g	53 mg
Tofu	1/2 C	10 g	25 mg

**Source:** Soyfoods Association of America, Soyfood Facts, [www.soyfood.org](http://www.soyfood.org). Soy protein and isoflavone levels may vary by product based on manufacturing process and the source of soy protein. Additional information on soyfood isoflavone content can be found at: Soy Isoflavone Database, [www.nal.usda.gov/fnic/foodcomp/Data/isoflav/isoflav.html](http://www.nal.usda.gov/fnic/foodcomp/Data/isoflav/isoflav.html).

*Cooking Basics.* Soymilk may be consumed as a beverage or substituted for dairy milk in most recipes. Culinary chefs prefer cooking with whole soymilk to provide firmer consistency in cooked dishes such as puddings and custards.

*Soymilk Tips.* Soymilk can be used in almost any way that cow's milk is used:

- Use soymilk to make cream sauces or soups that are cholesterol-free and low in saturated fat.
- Create your own delicious shakes with soymilk, soy ice cream or tofu, soy yogurt, and fruit.
- Try soymilk instead of evaporated milk to produce lower-fat custards and pumpkin pies.

## Soy Flour

*Product Description.* Soy flour is made from roasted soybeans that have been ground into a fine powder. Full-fat soy flour contains the natural oils that are found in the soybean; in defatted soy flour, the oils are removed during processing. Both kinds of soy flour will give a protein boost to recipes; however, defatted soy flour is even more concentrated in protein than full-fat soy flour.

*Storage.* Full-fat soy flour should be stored in the refrigerator or freezer to preserve its freshness. Defatted soy flour may be stored on the shelf.

*Cooking Basics.* Soy flour tends to pack down in a container, so always stir or sift before measuring. Baked products containing soy flour tend to brown more quickly, so you may want to lower oven temperatures slightly.

*Substituting Soy Flour.* Because soy flour is free of gluten, which gives structure to yeast-raised breads, it cannot replace all the wheat or rye flour in bread recipes. However, using 15% soy flour in a recipe produces a dense bread with a nutty flavor and a moist quality.

Place 2 T soy flour in your measuring cup for every cup of wheat flour before measuring all-purpose or other flour called for in the recipe.

In baked products, such as quick breads, that are not yeast-raised, up to 1/4 of the total amount of flour in the recipe can be replaced with soy flour. For each cup of flour called for, use 1/4 C soy flour and 3/4 C all-purpose or whole wheat flour.

*Soy Flour Tips.* In your own kitchen, use soy flour to thicken gravies and cream sauces. Premix a batch of 1 part soy flour and 3 parts wheat flour so that it is ready to use when you bake.

## Soy Protein Powder

*Product Description.* If you want to eat the most soy protein per serving in your meals, then try adding some soy protein isolate powder in your favorite recipes.

Soy protein isolate is a dry powder food ingredient

that is made from defatted soy flakes. Containing 90% protein, soy protein isolates possess the greatest amount of protein (*see Table 1*) and all the essential amino acids of all soy products.

Soy protein isolate powder is sold in canisters in health food sections of stores. It's often labeled as "soy protein powder drink mix." Most soy protein powder drinks on the market are made with soy protein isolate.

Soy protein powders come in plain, vanilla, chocolate, and strawberry flavors. Several brands are fortified with calcium.

*Storage.* Kept sealed and dry, it is shelf-stable for many months. Look for use-by dates on the container.

*Recipe Ideas.* Be sure to read the nutrition label of your soy protein powder for the protein level/serving.

- Add a serving of plain soy protein isolate to your favorite soup. Remove a small amount of hot soup and blend it with isolate powder. Add the mixture to the soup.
- Mix a serving of flavored soy protein shake powder with cold juice, milk, or soymilk.
- Mix a serving of soy protein powder into your favorite hot cereal.
- Try mixing soy protein powder to your favorite salad dressings or sauce for extra protein.

## Soy Meat Alternatives

*Product Description.* Meat alternatives (also called meat analogs) are non-meat foods made from soy protein and other ingredients mixed together to simulate various kinds of meat. Flavors include pork, beef, poultry, and sausage.

*Where to Find.* Look for meat alternatives in grocery stores in the following locations:

- Refrigerated case: beef and sausage-style crumbles, deli slices, burgers, wieners, entrées, taco filings.
- Freezer case: burgers, crumbles, sausage-style links and patties, chicken-like strips.
- Dry, prepared foods (dry mixes and shelf-stable): taco filings, sloppy joes, chili, meatball and loaf mixes, sausage-style strips, and texturized vegetable protein.

*Storage.* Frozen or refrigerated meat alternatives should be stored accordingly at home. Others come in dry-mix boxes and may be stored on the shelf.

*Cooking Basics.* Follow package directions. Substitute a meat alternative for all or part of the meat in your favorite recipe.

*Recipe Tips.* Meat alternatives usually can be used the same way as the foods they replace, such as tofu hot dogs or soy burgers on the grill (*see Table 2*).

- Using meat alternatives in highly seasoned dishes, such as tacos, minimizes the flavor difference

between them and meat.

- One 12 oz package of soy burger-style crumbles is equal to 1 lb of ground beef.
- Substitute a package of soy burger-style crumbles for ground beef when preparing your favorite spaghetti, sloppy joe, chili, stroganoff, or hamburger casserole recipes.

### Whole Soybeans (dry, canned, green)

*Product Description.* Soybeans can be purchased as dry whole soybeans, canned yellow or black soybeans, and green (fresh or frozen) and shelled or in the pod.

Green vegetable soybeans (also called edamame) are harvested at 80% maturity. Edamame soybeans are a special bean variety that are bigger and sweeter than traditional soybeans grown in fields by most farmers. Cooked and lightly salted, these little green beans are a popular snack in Asia. These beans often are sold in the freezer section of natural food stores and should be stored in the freezer. Fresh beans, purchased in the pod, should be cooked and stored in the refrigerator.

*Whole, Dry Soybeans.* Soybeans are harvested when they are fully mature and dry. As soybeans mature in the pod, they ripen into a hard, dry bean. Whole dry soybeans can be found in grocery and health food stores.

Most soybeans grown in fields by farmers are smaller than food-grade beans used to make tofu and soymilk. Field beans may be cleaned and used in recipes after they have been soaked and cooked.

Do not eat soybeans raw. Soybeans must be cooked to

destroy the protease inhibitor found in soybeans. Heat treatment is necessary to decrease the activity of the inhibitors and improve the digestibility of the proteins.

*Storage.* Dry soybeans can be stored in an airtight container for long periods of time. Cooked soybeans, both yellow and black, are available in cans in natural food stores.

*Cooking Tips.* Substitute canned soybeans (white or black) in your favorite recipes that call for beans. Substitute green cooked soybeans in recipes that call for green peas or beans.

- Do not add salt or acidic ingredients (such as tomatoes, lemon juice, or vinegar) to yellow soybeans until they are thoroughly cooked. Acidic products delay the softening process. However, you may add these ingredients when cooking black soybeans to help them retain their shape.
- One 15 oz can of white or black soybeans is equal to 1 1/2 C of cooked soybeans.

*Cooking Dry Soybeans.* Remember that 1 C dry beans = 2-3 C cooked beans.

- Soak soybeans in 4 C water for each cup of beans for 8 hours or overnight. If you soak beans longer than 8 hours, place them in the refrigerator.
- Drain and rinse the beans, then add 4 C of fresh water for each cup of beans you started with.
- Bring to a boil, reduce heat, and skim off excess foam. Simmer about 3 hours, adding more water as needed, until beans are tender. They will remain somewhat firm compared to cooked navy beans.

<b>Food Ingredient</b>	<b>Soy Food Substitution</b>	<b>Serving Size</b>	<b>Fat Saved</b>	<b>Cholesterol Saved</b>	<b>Calories Saved</b>
Ground beef, 83% lean	Soy crumbles	3 oz	18 g	71 mg	98 kcal
Cheddar cheese	Soy-based cheddar cheese	1 oz	4 g	30 mg	36 kcal
Dairy, whole milk	Regular soymilk or regular reconstituted soymilk	8 oz	4 g	33 mg	70 kcal
Chicken breast, skinless	Soy chicken-like meat	3 oz	3 g	41 mg	72 kcal
Sour cream	Tofu sour cream	1 T	2.5 g	5 mg	19 kcal
Egg (as a leavening agent)	1/4 C silken "lite" firm tofu, mashed	1 egg equivalent	4.5 g	213 mg	53 kcal
Ricotta cheese, part skim	Tofu, firm, mashed to ricotta consistency	1 T	0	5 mg	0
Bologna	Soy bologna-style meat	1 slice	8 g	15 mg	80 kcal
Hamburger	Soy burger	1 pattie (38 g)	10 g	43 mg	70 kcal
Chocolate ice cream	Chocolate soy frozen dessert	1/2 C	3 g	22 mg	13 kcal
Hot dog	Soy hot dog	1 link	14 g	35 mg	90 kcal
Peanuts	Soynuts	1 oz	14 g	0	30 kcal
Peanut butter	Soynut butter	1 T	5.5 g	0	85 kcal

*Sources:* USDA Human Nutrition Service, Agriculture Handbook, #18-16, Composition of Food, Legumes and Legume Products; and product information.

*Pressure Cooker Method.* Soybeans may also be prepared using a pressure cooker.

- Place presoaked (8-12 hours soaked), drained, and rinsed beans in a pressure cooker.
- Add 4 C water plus 2 T of cooking oil for the first cup of beans and 3 C of water and 2 T of vegetable oil for each additional cup of beans (oil controls foaming).
- Do not fill the cooker above the halfway mark. Cook with 15 lb pressure for 9-12 minutes.
- Release the pressure inside the cooker and drain beans immediately.

## Textured Soy Protein

*Product Description.* Textured soy protein is one of the most economical soy protein sources on the market. It's made from defatted soy flour or soy protein concentrate that is compressed and extruded into granules or chunks. It is sold as a dried, granular product. When rehydrated with water, textured soy protein has a texture similar to ground beef or other meat products.

*Where to Find.* Textured soy protein is not always easy to find in the supermarket. It's normally carried in natural food stores in the bulk food area or the flour section. Because it is a dry product, you can find mail-order companies on the Internet that sell it.

*Storage.* Textured soy protein has a long shelf-life. Stored in a tightly closed container at room temperature, it will keep for several months. Once it has been rehydrated, store the textured soy protein in the refrigerator and use it within a few days.

*Cooking Basics.* Read the package directions for rehydration. When using textured soy protein in soups and sauces, you do not have to rehydrate it before use—just be sure the recipe has enough liquid. Texture soy protein chunks should be simmered a few minutes before using.

*Recipe Tips.* Use textured soy protein to replace all or part of the ground meat in almost any recipe. Replace one-fourth of the ground beef in meat loaf or burgers.

- Generally, textured soy protein will triple in volume when hydrated. For example, 1 lb dry textured soy protein will yield about 3 lbs hydrated textured soy protein.
- For 1 lb ground beef, substitute 1 1/2 C dry textured soy protein and hydrate with 1 1/2 C water.

## Tofu

*Product Description.* Tofu is probably the most versatile soy food to use in cooking. Also known as soybean

curd, tofu is a soft, cheese-like food made by curdling fresh, hot soymilk with a coagulant. In recipes, tofu acts like a sponge and has the ability to soak up any flavor that is added to it.

*Types of Tofu.* Two main types of tofu are available in American grocery stores.

- Water-packed (extra-firm, firm) tofu is dense and solid and maintains its shape well in stir-fry dishes, soups, or on the grill. Water must be squeezed out before using.
- Silken (extra-firm, firm, soft, reduced-fat) tofu is made by a slightly different process that results in a creamy, custard-like product. Silken tofu works well in puréed or blended dishes.

*Storage.* Tofu most commonly is sold in water-filled tubs, vacuum packs, or in aseptic brick packages. Unless it is aseptically packaged, tofu should be kept cold. Once the tofu package is open, it should be rinsed and covered with fresh water for storage. Change the water daily to keep it fresh, and use the tofu within the week.

Tofu can be frozen for up to five months. The texture will be spongy, chewy, and more meat-like. After thawing, store tofu in the refrigerator, and squeeze out excess water before using.

*Recipe Tips.* Tofu's versatility is reflected in the recipe ideas below.

- Replace all or part of the cream in creamed soups with silken soft tofu.
- Substitute puréed silken soft tofu for part of the mayonnaise, sour cream, cream cheese, or ricotta cheese in a recipe. Use it in dips and creamy salad dressings.
- Mix one box instant pudding mix, 1 1/2 C soymilk, and 10 oz of silken tofu for dessert. Chill for 2 hours.
- Crumble tofu into a pot of spicy chili sauce.
- Cubes of firm tofu can be added to any casserole or soup.
- Slices of extra-firm tofu can be baked on a broiler pan at 375° F for 20-25 minutes. Marinate slices in your favorite sauce for extra flavor.
- Substitute 1/4 C soft tofu for 1 egg in your favorite brownie mix.

*Tofu Pressing.* To reduce the amount of water in water-packed tofu, place block of tofu on an inverted pie plate or shallow dish. Stack another plate on top of the tofu. Add weight to the plate (use more dishes or canned goods) and wait 15-20 minutes; then pour off water.

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